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NECATOR AMERICANUS IN NATIVES OF THE PHILIPPINE ISLANDS.[1]

By CLARENCE L. COLE.[2]

In the routine examinations of patients admitted to the United States Army Hospital at Manila, P. I., many members of Philippine Scout organizations and native civilian employees have been found to have a few ova of *Uncinaria* in their stools. In these cases the presence of *Uncinaria* has not made itself manifest clinically to such an extent that a diagnosis of uncinariasis has often been made, and as many of these patients have been admitted from temporary stations in the field, where microscopical examinations could not be undertaken, they were therefore sent to the hospital accompanied by a different diagnosis. It has been customary to accept *Uncinaria* ova as belonging to the Old World species, without studying the adult parasites obtained after the administration of vermicides to those patients whose stools have shown ova, because of the fact that no other varieties of *Uncinaria* have been reported from the Philippine Islands.

In September, 1906, a private of the Twenty-eighth Company, Philippine Scouts, was admitted to the Division Hospital, Manila, P. I., and ova of *Uncinaria* were found in his stool, they being more abundant in

[1] Read at the Fourth Annual Meeting of the Philippine Islands Medical Association, Manila, February 28, 1907, with the permission of the chief surgeon, Philippines Division, Manila, P. I.

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ase than in any other which had been examined i[n] the prec[e]
nths. Three or four ova could be observed in the field at one time
the ⅔ objective was used. A very few *Uncinaria* were recovered in
st stools after the administration of thymol; two days later, follow-
course of thymol, about ninety were obtained and ova were
und again until fifteen days had elapsed, when, after a third course
drug a large number of *Uncinaria* (possibly fifty) were again
red. No more ova were encountered in the stools of this patient
Uncinaria obtained from this case corresponded quite closely in
rements to those given by Stiles[3] for the variety of *Uncinaria*
bed by him and to which he has given the name *Uncinaria ameri-*
(*Necator americanus*).[4] When examining the female of this
y the position of the vulva was noticed as one of the first things
ntiating *Necator* from *Agchylostoma*. In all the specimens ex-
d it has been found to be near the anterior one-third of the body
, figs. 1 and 2.) From these facts it appears that the specimens
ecator americanus. In the meantime, similar *Uncinaria* had been
red from other patients. The medical publications reaching Ma-
uring the progress of this work established the fact that *Necator*
canus had been identified in material from Guam and China.[5]
interest had been aroused by the supposed finding of *Necator*
canus in natives of the Philippine Islands, great care was taken
ure as much material as possible for comparison. In addition to
tient mentioned above, seven other Filipino and two American sol-
have been found to harbor this parasite. The stations of these
rs were widely separated and in different islands of the Archipel-
s follows: four from the same station as the case just referred to
rom the Island of Samar, another from the city of Manila,
ican soldier was sent to this hospital from the Island of Guimar
her from Camp Daraga, Luzon. No less than five hundred *Un*
have been collected from these cases.[6]
structures which are constantly present and unmistakable
Uncinaria, which resemble *Necator americanus* more than they d
her of the *Strongyloidæ*, were thought to be of sufficient imp

H. & M. H. S. Bull. (1903), No. 10.
Young Stage of the American Hookworm—*Necator America*
–8 to 12 Days after Skin Infection in Rabbits and Dogs. Stile
Am. Med. (1906), 11, 63.
ll. Johns Hopkins Hosp. (1906), 17, 313.
otomicrographs and camera-lucida drawings have been mad
imens, to assist in demonstrating the presence of the newly
nd in the descriptions or illustrations by Stiles;
gans, or their homologues, were illustrated by the
duodenale. (After Schulthess (copied from Blan

to form the basis for the supposition that a new species of *Necator* had been found in the Philippine Islands.

About the time this conclusion had been reached and an effort had been made to describe this supposedly new variety of *Uncinaria*, it appeared that others were finding species of *Necator* differing from *Necator americanus*.

Stephens [7] thinks that *Necator americanus* may be only one of many species which exist in different parts of the world. He has found varieties of *Necator* differing from *Necator americanus* in material collected in Burma and Assam. Loos [8] of Cairo confirmed Stephens's statement and identified at least three different species in the material which the latter had collected. It is not known upon what characteristics Stephens bases his differentiation as no specimens have been described by him.

In January, 1907, through the kindness of Lieut. P. E. Garrison, United States Navy, medical zoölogist at the Bureau of Science, an opportunity was given to compare the *Uncinaria* I had obtained with type specimens of *Necator americanus* which he had procured in Washington from Stiles. They were found to be similar.[9]

After quoting the description given by Stiles for *Necator americanus* I will attempt to demonstrate by means of drawings and photomicrographs the characteristics of the *Uncinaria* found here.

The New World hookworm of man, *Uncinaria americana* Stiles, 1902.

Specific diagnosis.—Uncinaria: Body cylindrical, somewhat attenuated anteriorly. Buccal capsule with a ventral pair of prominent semilunar plates or lips, similar to *U. stenocephala*, and a dorsal pair of slightly developed lips of the same nature; dorsal conical median tooth projects prominently into the buccal cavity, similar to *Monodontus;* one pair of dorsal and one pair of ventral submedian lancets deep in buccal capsule. Male, 7 to 9 millimeters long; caudal bursa with short, dorsomedian lobe, which often appears as if it were divided into two lobes, and with prominent lateral lobes united ventrally by an indistinct ventral lobe; common base of dorsal and dorso-lateral rays very short; dorsal ray divided to its base, its two branches being prominently divergent and their tips being bipartite; spicules long and slender. Female, 9 to 11 millimeters long; vulva in anterior half of the body, but near equator. Eggs, ellipsoid, 64 to 76 μ long by 36 to 40 μ broad, in some cases partially segmented in utero, in other (rare) cases containing a fully developed embryo when oviposited.

Habitat.—Small intestine of man (*Homo sapiens*) in America (determined to date (1902) for Virginia, North and South Carolina, Georgia, Florida, Alabama, Texas, Porto Rico, Cuba, and Brazil).

[7] *Indian Med. Gaz.* (1906), 41, 398.

[8] *Ibid.*

[9] The single male specimen of *Necator americanus* which was given me had been mounted for some time, and as a result of the pressure of the cover glass the specimen is flattened and can not be placed in as favorable position for demonstrating the structures in question as some of the fresh ones from the Philippines.

4.4 millimeters. No. 3: Length of worm, 12.6 millimeters; distance from head to vulva, 5.5 millimeters.

The ratio which the length from head to vulva bears to the length from the vulva to the tip of the tail in the three cases above given is as follows:

No. 1, 1: 2.32. No. 2, 1: 2.43. No. 3, 1: 2.29.

The ova are larger than those of *Uncinaria duodenalis*. (Pl. IV, fig. 2.) Harris [10] reports the measurements of ova of *Necator americanus* from 57.5 to 80 μ in length and 35 to 52.5 μ in breadth; and the average from a large number of ova as 66.52 μ in length by 42.53 μ in breadth. In these cases the ova measured from 58 to 73 μ in length by 36 to 46 μ in breadth. The average measurement of 40 ova was 66 by 40 μ.

The attention of the commanding officer of the Division Hospital, Major F. J. Ives, United States Army, having been invited to the number of patients from the Twenty-eighth Company of Philippine Scouts admitted to the hospital and infected with *Necator americanus*, he requested the chief surgeon of the Philippines Division to authorize an investigation. The result was that *Uncinaria* ova were found in the first slide from 13 of 25 men (52 per cent) examined, who at that time were on duty.

The fact that *Necator americanus* has been recovered from the stools of all enlisted men showing *Uncinaria* ova, admitted to this hospital since September, 1906, and that ova corresponding in measurements to those of *Necator americanus* have been found in the stools of 52 per cent of the men examined in one company, would lead one to think that a large percentage of natives of the Philippine Islands harbor this parasite. Craig [11] reported cases of uncinariasis in soldiers who had returned from the Philippine Islands to the United States, but in those only *Uncinaria duodenalis* was found.

As both varieties of *Uncinaria* are present in the Philippine Islands and as these investigations demonstrate that *Necator americanus* is quite prevalent, uncinariasis would appear to be one of the most common diseases to be found here and it would be expected that many severe cases would be encountered.

Seventy-six officers and men of the Regular Army have been treated for uncinariasis in the Division Hospital since its organization in 1898, and of this number only 38 were admitted with a diagnosis of uncinariasis or ankylostomiasis. The histories of these 38 patients show gastro-intestinal disturbance in 32, anæmia in 6, heart murmurs in 2. Dyspnœa and œdema were not noted among the symptoms in any of them. Six cases were uncomplicated by other diseases; 21 were suffering with dysentery as well as uncinariasis; 5 with diarrhœa; 5 with malaria; 1

[10] Uncinariasis (Ankylostomiasis); Its Frequency and Importance in the Southern States. *The Atlanta Journ.—Record of Medicine* (1903).

[11] The Occurrence of Uncinariasis (Ankylostomiasis) in Soldiers of the United States Army. *Am. J. Med. Sci.* (1903), **126**, 798.

with sprue; 3 with filariasis; 1 with rheumatism; 1 with liver abscess, and 1 with epilepsy.

Thirty-eight cases have been admitted to the hospital for other conditions, and ova of *Uncinaria* have subsequently been found in their stools. The diagnosis in nineteen of these has been changed to uncinariasis with no complication. In nearly all of the others gastro-intestinal disturbance was marked; anæmia being observed in five. Of the remaining cases, dysentery, tuberculosis and malaria were common complications. Three of these were diagnosed as beriberi and in one the diagnosis was changed to uncinariasis.

I have not had an opportunity during my tour of duty in these Islands to travel through the country districts where one would expect to find conditions most favorable for the development of *Uncinaria* and to encounter the most serious cases of uncinariasis. The patients I have had an opportunity to examine and the records of cases to which I have been able to refer, have all been of soldiers who had not more than three years previously passed a rigid physical examination. These men had only been exposed to the infection during longer or shorter periods of active service in the field, but some of the Scouts may have been suffering from mild infections of a number of years' duration.

In the United States it has been found that women and children are the greatest sufferers, except in the cases where the employment of the men caused an exposure of the bare skin to the contaminated earth. Soldiers are exposed to infection by this parasite while performing field service and then only during the rainy season. It would hardly be possible that cases as severe would be found among these picked men as among natives in a barrio.

The health of the soldier in garrison is safeguarded by all the precautions known to the sanitarian; it would be a grave condition indeed if under these circumstances severe cases of uncinariasis could develop at all and it could hardly be possible for a severe infection to occur in any great number of soldiers during the short tours of field duty which are customary in these Islands.

In the provinces no precautions at all are taken properly to dispose of the waste. Privies and vaults are among the rarities and the surface of the ground around by far the greater majority of the houses has been contaminated from the time that the houses were built. The abundant growth of vegetation around dwellings furnishes the most favorable conditions (shade and moisture) for preserving the vitality of rhabditiform embryos, and the barefooted householder and his family are constantly exposed to the infection.

I wish to quote a few lines from Ashford[12] in regard to the severity of this disease in Porto Rico:

> There seems to be no doubt that for many years from 5,000 to 7,000 people have been dying annually from this easily curable and preventable disease; nor is it an exaggeration to say that the great majority of those affected with *Necator americanus* are physically incapable of rendering anything like their full quota of labor. * * * Fully 70 per cent of the worm carriers suffer more or less severely from their infection, and an incredibly large number of men that should form the bone and sinew of this healthful and beautiful island are ghost-like invalids, compelled to work, though sick, that their families may not starve.

If such a condition exists in Porto Rico why should not a similar one be found in the Philippine Islands where we have the same parasite, all the favoring conditions for its growth which a tropical climate affords and a population whose habits are such that the greatest care could not facilitate the dissemination of the infection more perfectly?

There are two conditions existing in Porto Rico which have been found favorable for the spread of uncinariasis that are dissimilar in these Islands. They are:

First. An occupation in which a large number of barefooted people are gathered together during the rainy season, and each by his careless habits increases the danger to the others.

Second. The Porto Ricans are a lighter skinned race than the Filipinos.

In the Philippine Islands the cultivation of coffee is not a very extensive industry and the number of people engaged in it is comparatively small. There is no single industry in which great numbers of the Filipinos are engaged that presents equally favorable opportunities for universal dissemination of the infection. Nearly every writer upon uncinariasis states that the Negro living in localities where uncinariasis is prevalent does not suffer from the anæmia which lighter skinned people are subject to. The Filipino being quite dark skinned may be less susceptible than the Porto Rican.

For many years authorities have considered the Porto Rican anæmia to be due to an innutritious diet. The Porto Rican Anæmia Commission proved the fallacy of this supposition by restoring thousands to health by removing the *Uncinaria* with which the poorer people were infected. One would not expect the poor negro of our Southern States or of Porto Rico to subsist upon a more nutritious diet than the poor white of the same locality; yet many investigators have observed the relative infrequency of severe cases of anæmia in the negroes of these districts.

[12] *Military Surg.* (1907), **20**, 41.

CONCLUSION.

The points which I wish to emphasize as a result of these investigations may be summarized as follows:

Necator americanus is a common parasite in natives of the Philippine Islands.

This infection occasions a great loss of time to the Government through illness of the enlisted men, principally from the Scout organizations.

There is an unnecessary increase of expense for medicines and hospital supplies because of this condition.

Every man infected with *Uncinaria* is a menace to his comrades and a source of danger to the community in which he is stationed.

No person suffering from uncinariasis, mild or severe, is capable of performing his duty as efficiently as one who is free from this infection.

Everyone suffering from uncinariasis, although it may be mild, is more susceptible to other diseases and having contracted a complicating disease, is more severely attacked because of his weakened condition and also his period of illness is necessarily longer.

Uncinariasis is a disease which yields readily to treatment, with little danger and with positive results. If uncinariasis is as prevalent in the Philippine Islands as the few examinations here reported would indicate, then there is no way in which the systematic expenditure of a small amount of money will bring a greater return in health, happiness, efficiency, and increased prosperity, than in its eradication.

ILLUSTRATIONS.

[*Photomicrographs by Mr. Charles Martin, photographer of Bureau of Science, Manila.*]

PLATE I.

FIG. 1. Female *Necator americanus*. (Original.) *A*, the vulva; *B*, the excretory pore; *C*, the anus.

2. Photomicrograph of female *Necator americanus*. Magnification, 14×1. *A*, excretory pore; *B*, vulva; *C*, anus.

3. Male *Necator americanus*. (Original.) *A*, excretory pore; *B*, *C*, dorsal rays; *D*, one of the precaudal papillæ.

4. High magnification of the excretory pore. *Necator americanus*. 400×1. (Original.)

PLATE II.

FIG. 1. Outline drawing of the tail of the male showing both precaudal papillæ, *Necator americanus*. (Original.)

2. Tail of the male, *Necator americanus*. (Original.) *A*, dorsal rays; *B*, dorsal leaflets of the lateral lobes of the caudal bursa; *C*, one of the precaudal papillæ; *D*, ventral enlargement of the caudal bursa; *E*, ventral lobe of the caudal bursa.

3. Illustration of the tail of the male *Necator americanus* showing the principal structures. (Original.) *A*, dorsal rays; *B*, dorso-lateral ray; *C*, lateral rays; *D*, ventro-lateral rays; *E*, spicules; *F*, ventral rays; *G*, ventral lobe of the caudal bursa; *H*, precaudal papilla; *I*, ventral prominence of caudal bursa.

4. Photomicrograph of tail of male *Necator americanus*. Magnification, 87×1. *A*, dorsal rays; *B*, precaudal papilla; *D*, the ventral lobe of the caudal bursa; *J*, barbed tips of the spicules; *K*, dorsal leaflets of lateral lobes of the caudal bursa; *R*, the ventral enlargement of the caudal bursa adjacent to the precaudal papillæ.

PLATE III.

FIG. 1. Photomicrograph showing precaudal papillæ of the specimen of *Necator americanus* given me by Dr. Garrison. Magnification, 106×1. *A*, precaudal papillæ; *B*, ventral enlargement of the caudal bursa adjacent to the papillæ.

2. Photomicrograph of male *Necator americanus*. Magnification, 10×1.

3. Outline drawing showing the ventral lobe of the caudal bursa folded between the lateral lobes, *Necator americanus*. (Original.)

4. Illustration of the tail of the male *Necator americanus* dorso-ventral position. *A*, dorsal rays; *B*, dorso-lateral rays; *C*, lateral rays; *D*, ventro-lateral rays; *E*, ventral rays; *F*, spicules. The precaudal papillæ are too delicate to be seen through the thick body.

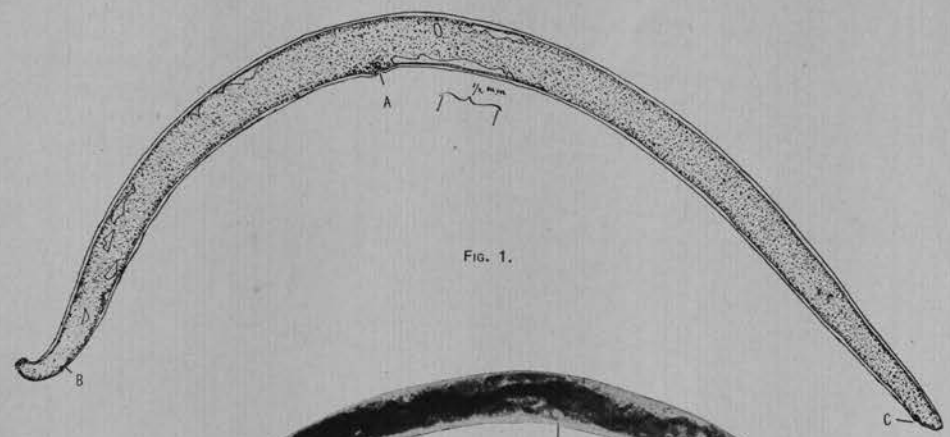
PLATE IV.

FIG. 1. Photomicrograph of tail of male *Necator americanus*, postero-ventrally. The same specimen illustrated by drawing. Magnification, 56×1.

2. Illustration of ten uncinaria ova in different stages of segmentation with their respective measurements. (Original.) *1*, 72×40 μ; *2*, 62×38 μ; *3*, 58×42 μ; *4*, 73×42 μ; *5*, 58×43 μ; *6*, 68×36 μ; *7*, 68×38 μ; *8*, 62×38 μ; *9*, 68×38 μ; *10*, 62×42 μ.

3. Photomicrograph of buccal plates in mouth of *Necator americanus*. Magnification, 46×1. *A*, large ventral plates; *B*, dorsal plates.

4. Tail of the female greatly enlarged, *Necator americanus*. (Original.) *A*, anus.



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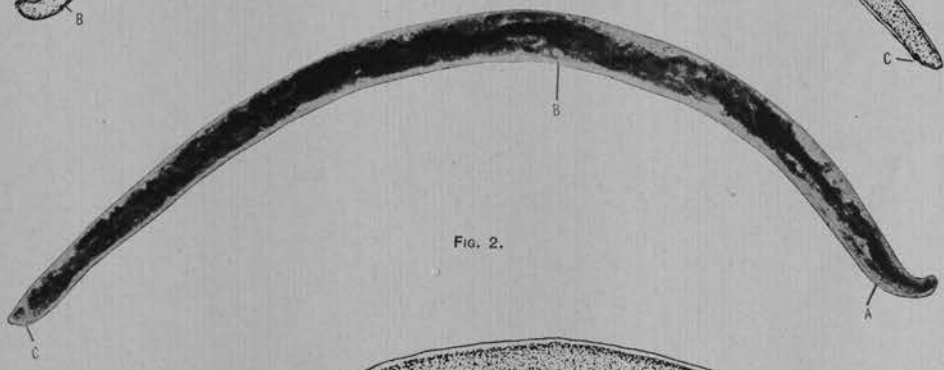
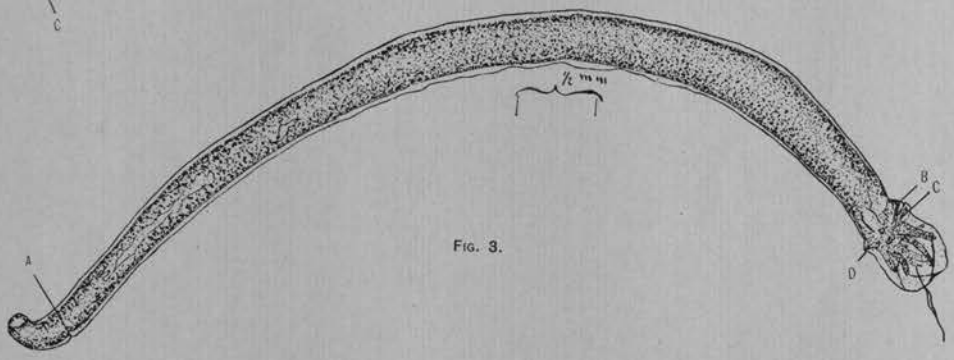


FIG. 2.



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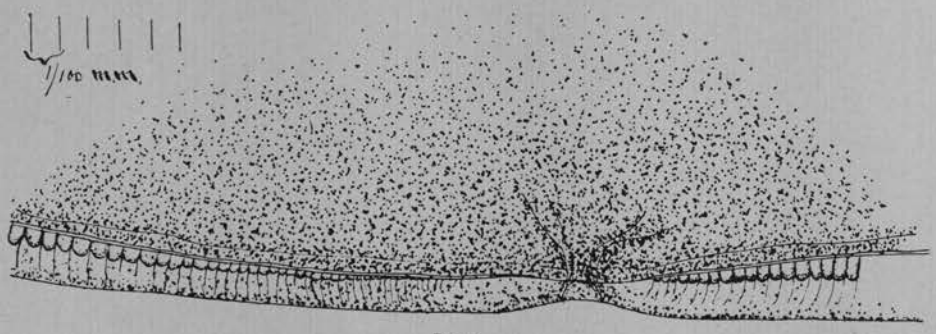
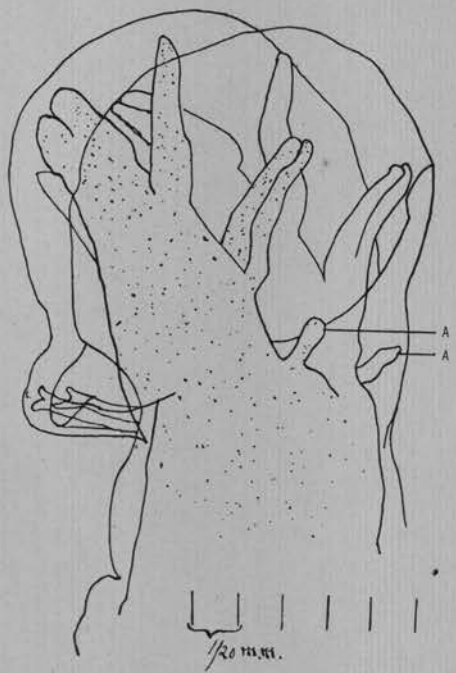


FIG. 4.

PLATE I.



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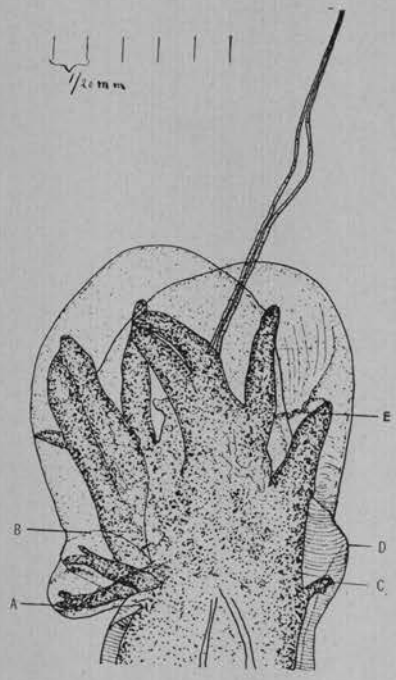

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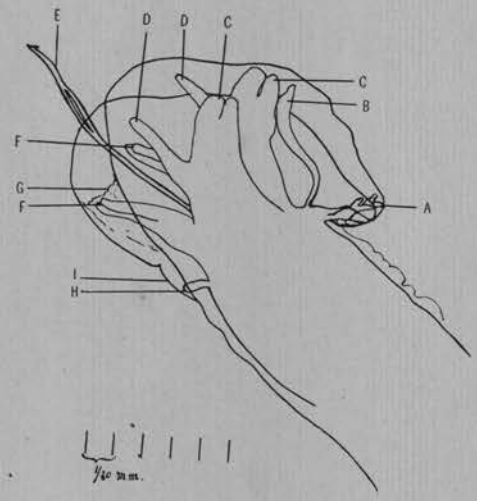

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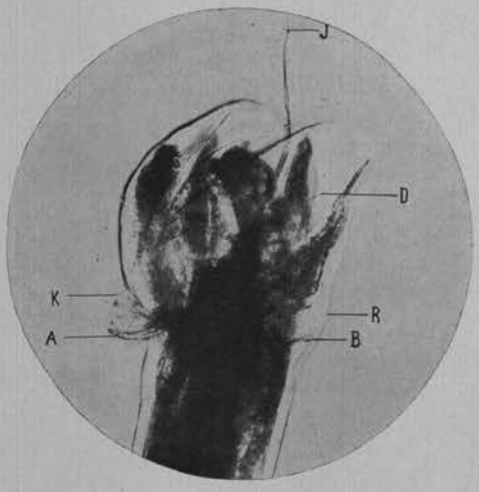

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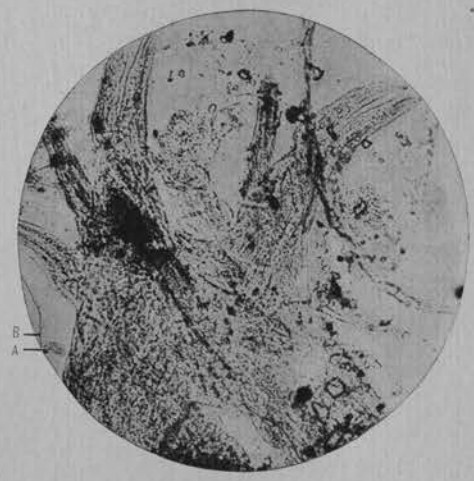

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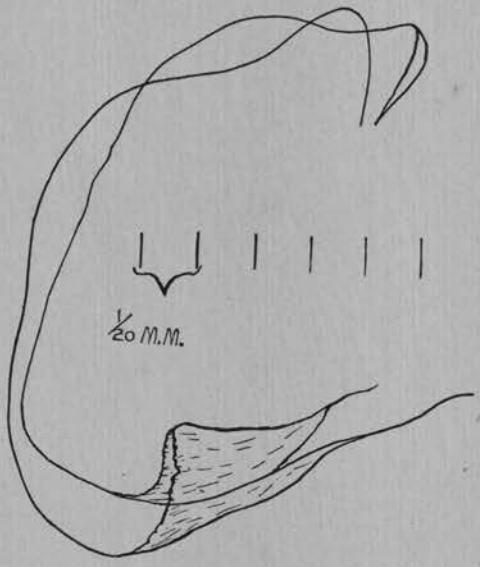

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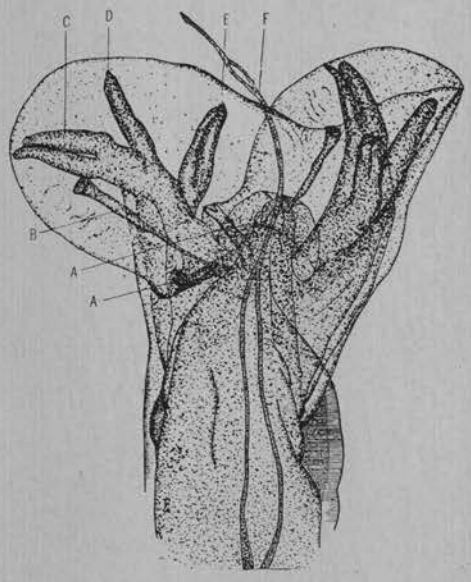
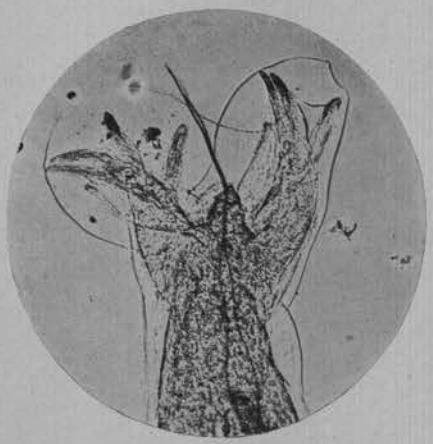


FIG. 4.

PLATE III.



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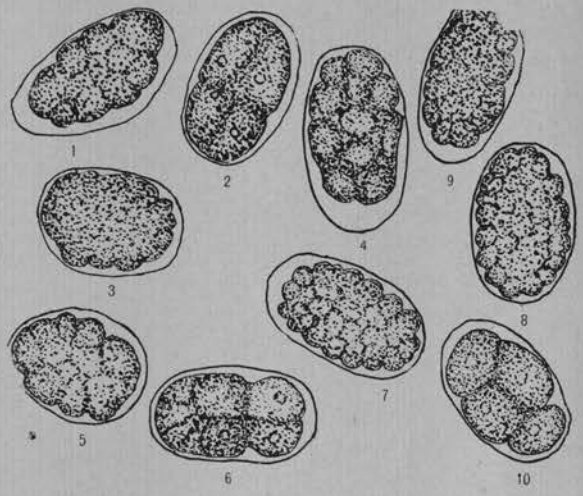

FIG. 2.

FIG. 3.

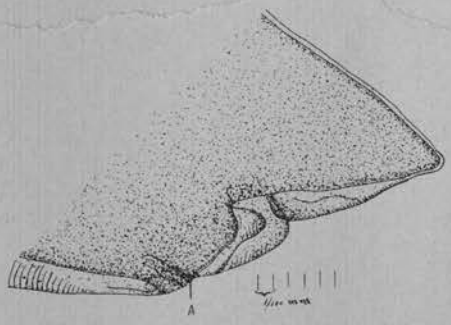

FIG. 4.

PLATE IV.

THE RECENT TREND OF IMMUNITY RESEARCH.[1]

By HARRY T. MARSHALL.
(*From the Biological Laboratory of the Bureau of Science, Manila, P. I.*)

The term immunity has come to have two meanings within recent years; it retains its older significance and it is also used broadly to designate the condition resulting when an organism has reacted to foreign albuminous material. Researches along the more general lines of immunity have led in such widely divergent directions that a general review of the literature can not be attempted within the limits of the time allotted to this paper. Therefore, I have selected for review two subjects, which possibly are somewhat fresher than the others and which are commanding considerable attention at present. We will consider first the phenomenon known variously as complement deflection, complement deviation, complement diversion or blocking of complement, and second, Bail's aggressin hypothesis of infection and immunity.

I. DEFLECTION OF COMPLEMENT.

Early in the course of Bordet's(3) and Ehrlich's(8) studies on the mechanism of hæmolysis, it was found to be possible to prevent by certain fairly definite procedures the union of complement with red corpuscles previously laden with immune body. The bearing of this phenomenon upon the receptor theory and its value as a demonstration of the receptor explanation of hæmolysis was discussed, and for the sake of simplicity the property possessed by a fluid of blocking the action of complement was attributed to a hypothetical substance termed "anti-complement." Subsequently, what appeared to be another type of the blocking occurring during bacteriolysis, was described by Neisser and Wechsberg(29).

We must remember that it never has been possible to obtain complement pure, and that it is defined only in part, the definition at present demanding (*a*) that complement shall be capable of uniting with attached amboceptors by the hypothetical haptophore group, and (*b*) that it shall, either by its own inherent energy, or by its mere presence, bring about destructive changes in the body to which it unites (red corpuscles, bacterium, etc.). These changes are tentatively described as being of

[1] Read at the Fourth Annual Meeting of the Philippine Islands Medical Association, Manila, March 2, 1907.

a fermentative or enzyme-like nature. The instability of complement is a more or less permanent characteristic, and equally characteristic are the facts that complement is normally present in varying amount in fresh serum, and that the quantity can not be influenced by the usual processes of immunization, provided the health of the animal remains unimpaired. If either of the first two characteristics fails, we have at present no means at our disposal of recognizing complement. A number of convincing arguments have been brought forward to prove that there are different complements in different serums, and also that any one specimen of serum contains a number of complements, although other observers claim that all forms of complement action are due to a single substance or form of energy in the serum. Whether complement has other actions we do not know, nor whether it is capable of uniting with a variety of other substances. Similarly, we do not know anything of anti-complement except the one fact that it prevents the action of complement. Whether a variety of substances or conditions could be the cause of such an inhibition was not determined at the time that anti-complements were first considered. Bordet(4) claims that specific anti-complements can be produced, the action of which is different from that occurring in complement deflection, and Marshall and Morgenroth(20) found it possible with a nonspecific anti-complement to block out certain definite complement activities from a serum without interfering with its other complement actions. On the other hand Pfeiffer and his colleagues (10:30) claim that the phenomenon of complement deflection explains reactions hitherto accounted for as the result of anti-amboceptor action.

The phenomenon of complement deflection was first described in 1901 by Bordet and Gengou(5) who found that hæmolysis was no longer produced in properly prepared corpuscles if the complement-containing fresh serum was previously added to a mixture of bacterial emulsion and specific anti-bacterial serum.

In 1905, Gay(11, 12, 13), in Bordet's laboratory, discussed this phenomenon, and concluded that the complement was removed by the union of specific precipitin with precipitable substance. He found, as Sachs(32) did also, that the immune body was not affected in this reaction, only the complement being removed. He attributed the well-known Neisser-Wechsberg phenomenon of deflection and the antilytic action of normal serum described by Pfeiffer and Friedberger, and the anti-complementary action of normal serum described by Sachs, to the same phenomenon of precipitation. He holds that the above-mentioned investigators overlooked minute traces of precipitable substance which remained attached to the corpuscles, etc., after one washing with salt solution, and which could be removed only by repeated washings.

Moreschi(22, 23), working independently of Gengou and Gay, obtained similar results. His experiments led him to conclude that our

ideas of complement must be revised extensively, both Ehrlich's and Bordet's hypotheses failing to account for the conditions which he met with. Pfeiffer and Moreschi(30) and Friedberger and he(10) supposed that the disappearance of complement was in some way brought about by the union of precipitin and precipitable substance and varied with the amount of precipitation. They found that deflection occurs not only *in vitro* but also *in vivo*. They concluded that the phenomena formerly explained as depending upon the action of anti-complements and anti-amboceptors are actually due to complement deflection.

Sachs(32), replying in 1905 to Gay, worked over some experiments of Pfeiffer and Friedberger and concluded that the phenomenon of deflection is not due to precipitation, but is a function of the union of amboceptor with its corresponding anti-genetic substance. The deflection occurs even when no precipitate is formed and varies independently of the amount of precipitate, a result also obtained by Klein(17). Wassermann and Bruck(35) also point out that old bacterial extracts no longer precipitate, but still deflect and that the same holds true of tuberculin and anti-tuberculin. The Neisser-Wechsberg studies and one by Lipstein also supports Sachs's contention.

From the first, the phenomenon of deflection has been used in practical diagnosis. Bordet and Gengou elaborated a delicate test for the demonstration of anti-bodies specific for various bacteria. Subsequently, in 1902, Gengou(15) widened the application of this method, making it available for the determination of the presence of anti-bodies for the most diverse albuminoid solutions, such as milk, egg, etc. Neisser and Sachs(26, 27) employed the test for recognizing not the anti-body but the antigen, using their technique with special success in detecting minute traces of blood, and being able from these traces to determine the species from which the blood was derived. They advise the adoption of the method in forensic medicine, to supplement the precipitin test, and make mention of three cases in which they employed it. The advantages of the deflection method are: First, that it acts as a control for the precipitin method; second, that hæmolysis is a much more definite index than minute precipitation; third, that an opalescent serum is available for use; fourth, that it is not necessary to have such high potency serum as is needed in the precipitin test and that it is not necessary to wait for the clearing of the serum, which is so tedious in the older test.

During the course of 1905 and 1906, Wassermann and his co-workers have given a new application to this technique. They found that dissolved bacterial substances could be detected as readily as bacterial emulsion (*Med. Klin.* '05), and they were able to demonstrate minute traces of bacterial substance in blood derived from individuals suffering from various infections. By modifying the technique they were also able to

recognize the early stages of reaction by proving the presence of minute traces of soluble anti-bacterial substances in diseased tissues. They then went one step further and made a novel application of this principle, applying it in the detection of minute traces of even unknown infectious agents in the infected body.

They perform the experiment in testing for anti-tuberculin and tuberculin in organs as follows:

A specific hæmolytic serum is first obtained and this is used with the corresponding anti-genetic blood corpuscles as an indicator of deflection of complement; for, if a specific serum and the corresponding red corpuscles are brought together and fresh serum is added, hæmolysis occurs if the fresh serum contains free complement, it does not occur if no free complement is present. Hæmolysis is therefore the index of whether or not free complement is present in the fresh serum. If a fresh serum which has been shown to contain complement loses its complementary action upon being treated with a mixture of tuberculin and anti-tuberculin, the complement is said to be deflected, provided suitable controls indicate that its disappearance is directly due to the union occurring between tuberculin and anti-tuberculin, and is not due to the tuberculin alone, to the anti-tuberculin alone, or to any other agent involved in the experiment.

It having been established that the union of tuberculin and anti-tuberculin deflects complement, any given tissue extract is tested for its content in tuberculin by noting whether the suspected extract and a stock preparation of anti-tuberculin will block the action of a serum known to contain active complement. On the other hand, a given tissue extract is tested for its content of anti-tuberculin by bringing together a stock preparation of tuberculin, the suspected extract and the complementary serum, and afterwards testing for hæmolysis.

The technique of the experiment is elaborate, a large number of controls are required and the test tubes must be scrupulously cleaned. The organs to be tested for tuberculin are removed under aseptic precautions and ground in a mortar with normal salt solution containing 0.5 per cent of carbolic acid. Five cubic centimeters of normal salt per 1 gram of organ are employed. The mixture is shaken in a machine for twenty-four hours at room temperature, centrifugalized clear of particles and the supernatant fluid drawn off and tested by mixing varying amounts with anti-tuberculin and fresh guinea pig serum. These three are brought together in a test tube and kept for one hour at 37° C. Finally, the mixture is added to test tubes containing 1 cubic centimeter of a 5 per cent suspension of serum-free sheep's corpuscles and twice the dissolving dose of inactivated rabbit's serum specifically hæmolytic for sheep's corpuscles. The volume of fluid in each tube is brought to 5 centimeters of salt solution. The test tubes are placed in the thermostat at 37° C. for two hours, are kept on ice over night, and in the morning are examined to determine the extent of hæmolysis which they may exhibit.

The technique in testing organ extracts for anti-tuberculin is the same, except that fixed quantities of a stock preparation of tuberculin and of complement are used with varying quantities of organ extract.

The following controls must accompany every test:

1. The organ extracts must be free from tissue particles, as these alone may bind complement.

2. The deflecting power of organ extracts alone and of tuberculin alone must be determined in the test for anti-tuberculin, and that of organ extract alone and of anti-tuberculin alone in the test for tuberculin. Occasionally, one of these substances exhibits a certain power of deflection.

3. The extract to be tested must be added to the sheep corpuscle-serum mixture to determine whether it alone effects hæmolysis.

4. A complete parallel series must be made at the same time, using nontuberculous organs from the species to which the test animal belongs.

5. The controls usual in every hæmolytic experiment must, of course, be set also—that is, sheep's corpuscles and salt solution; corpuscles and amboceptor; corpuscles and complement alone.

The hæmolytic dose of the specific rabbit's serum is determined in preliminary tests and likewise that of the complement serum. About twice the hæmolytic dose of amboceptor and the single dose of complement are employed in the experiment.[2]

Neisser and Sachs(28) state that deflection by serum and anti-serum fails if the anti-serum is first boiled, and they include a control with boiled anti-body in their forensic test. They also state that there is an optimum amount of the anti-serum causing deflection when added to complement and the suspended blood specimens. This amount is determined at a preliminary test in which varying amounts of anti-serum are employed with a fixed amount of complement, and a fixed amount (0.0001 cubic centimeter) of the test blood preparation. At first they recommended the employment of normal rabbit serum with sheep's corpuscles as the hæmolytic indicator, but later they advised the use of a specific serum with sheep's corpuscles.

The application of the deflection method by Wassermann and Bruck (35) to the study of tuberculosis apparently sheds light upon the bacterial and anti-bacterial reactions occurring in tuberculous individuals. In tuberculous organs and in the sera of animals treated with tuberculin, anti-tuberculin was demonstrated, while it was absent from the sera of thirteen patients at different stages of phthisis. They succeeded in demonstrating tuberculin also in the diseased organs. As the anti-tuberculin receptors are elaborated at the tuberculous focus, and as they usually

[2] For a clear description of the technique and of the controls necessary, see Wassermann and Bruck, *München. med. Wchnschr.* (1906), p. 2396, and Morgenroth and Stertz, *Virchow's Archiv.* (1907), **188**, p. 166.

remain sessile for a longer or shorter time, especially in human beings, it results that if a tuberculous patient receives an inoculation of tuberculin, nearly all of the substance becomes attached in the diseased focus, the tuberculin being concentrated from the plasma by the fixed anti-tuberculin, instead of being allowed to diffuse itself throughout the body fluids. The result of this concentration is that even a minute trace of tuberculin will produce the well-known tuberculin reaction.

A person inoculated with tuberculin will produce anti-tuberculin and eventually set it free, and possibly patients having had localized tuberculosis for a long time may also liberate anti-tuberculin into the circulation, although thirteen cases were negative. This circulating anti-tuberculin prevents the action of a subsequently inoculated dose of tuberculin. This fact accounts for the uncertainty of the tuberculin reaction in the more chronic cases of tuberculosis.

The amount of circulating tuberculin varies in individuals and in species. It was easiest to obtain an anti-tuberculin serum from cattle, next from guinea pigs, and most difficult to obtain it from human beings. Wassermann and Bruck claim that tuberculous cattle intended for importation into Germany are previously inoculated with tuberculin so that they will not react to the official tuberculin test.

Bruck(6) was able to demonstrate the tuberculin in the circulation five days after the onset of severe symptoms, during the course of acute general miliary tuberculosis, and again on the eighth day. On the twelfth the circulating tuberculin had disappeared and the serum contained anti-tuberculin, the patient's condition at the same time being improved. Finally, shortly before death, the anti-tuberculin disappeared and tuberculin was again demonstrable.

Bruck found the deflection test equally satisfactory in the diagnosis of pleural exudates, of the spinal fluid in meningococcus infection, of serum from typhoid fever patients, and in gonococcus infections(7). He states that Bockenheimer and Lexer could diagnose streptococcus sepsis and erysipelas by this method. A further study of meningococcus infection and immunity was made along these lines by Kolle and Wassermann(18). Müller and Oppenheim(21) also applied this test successfully in gonorrhoeal arthritis, Koch and Bruck in meningitis, and Eitner(9) in diagnosing leprosy.[3] Finally, Wassermann, A. Neisser, and Bruck(36) obtained a serum from monkeys immunized with syphilitic material and were able to obtain the specific deflection reaction with fresh extracts from syphilitic tissue, whereas the reaction was absent when fresh extracts of normal organs were employed. This result was

[3] Salomon, *Wien. med. Wchnsch.* (1907), **75**, 121, found the method of no value in the diagnosis of cancer.

confirmed later(25)—from 70 to 75.5 per cent of 163 cases giving a positive result either for syphilitic virus or for anti-syphilitic reaction product. They could demonstrate the virus in the blood of patients taking mercury. The anti-bodies were particularly abundant in the spinal fluid. Wassermann and Plaut(37) employed this last fact in the investigations of various paralyses. They found that the spinal fluid from a certain number of paralytics contained anti-syphilitic material which acted with fresh extracts of syphilitic organs to deflect complement. In some cases the spinal fluid of a paralytic had slightly greater deflecting action than his serum.[4] Wassermann(34) notes further that the test is available for the diagnosis of protozoön infections.

The results obtained by Wassermann and his colleagues with this method are certainly extremely interesting, in fact, almost startling, but the work in other laboratories has not yet given that confirmation to the claims of Wassermann which justifies us in accepting them unreservedly. The criticisms have to deal with the mechanism of the phenomenon on the one hand, and on the other, with its practical value in diagnosis. Furthermore, the application of this method in each particular infection raises a certain number of special questions.

The two principal hypotheses to explain the deflection have been outlined above. Weil and Nakayama, Axamit(1) and F. Mayer (quoted by Ranzi(31)) object to the test *in toto*, claiming that deflection can be produced by mixing a complement serum with bacterial extracts alone without any anti-bacterial serum; Weichardt(38) adds that deflection can be produced by electrolysis and by heat, and Uhlenhuth(33) found that disappearance of complement can be brought about by diverse substances producing mechanical precipitation, while Landsteiner and Stankovic(19) obtained similar results with colloidal suspensions. It has been observed that albuminous solutions in general absorb complement, in amounts proportional to the quantity of albumin. Wassermann and Plaut recently remarked upon the unaccountable and rapid alterations in deflecting power occurring in the extracts ready for use in the experiment and upon the differences between various extracts, suggesting that these differences and the sediment gradully forming in even the clearest extracts are autolytic in origin. They speak also of the need of determining that the total amount of albumin in the various mixtures is not sufficient to deflect complement, and they suggest that only extracts be used which in 0.1 cubic centimeter doses, cause no deflection.

Moreschi(24) has recently concluded that the test is not sufficiently

[4] Recently the value of this method in diagnosis of syphilis has been confirmed by A. Schutze, *Berl. Klin. Wchnsch.* (1907), 126, and by Marie and Levaditi, *Ann. de l'Inst. Pasteur* (1907), XXI, 138.

delicate for the diagnosis of typhoid bacilli, as the bacilli alone are apt to cause deflection.[5]

Furthermore, it has been claimed by Ganghofner and Langner(14) that deflection varies according to the amount and concentration of the ingredients and that an excess of hæmolytic amboceptor and of complement destroys the results. The same writers, although they find the reaction a very sensitive one, conclude that it is not adapted to the purposes of clinical diagnosis owing to the many uncertainties inherent in such a complicated procedure.

Gengou(16) tested the value of the phenomenon as a means of diagnosing tubercle bacillus, using a dozen different acid-fast bacilli for comparison. He concluded that there was nothing specific about the reaction, and found that serum from an animal immunized against one acid-fast bacillus gave the deflection test when employed with other species of acid-fast bacilli.

Neisser and Sachs(28), replying to Uhlenhuth's objections to their forensic test for human blood, emphasize clearly the necessity of numerous controls as a basis for judging the results obtained by this method and they show that Uhlenhuth neglected one control, namely, the testing of the deflecting power of the boiled specimen. They say that it remains for experience to demonstrate whether there are nonspecific deflections which will make the test valueless. The negative results of Uhlenhuth, and of Gengou are possibly due to incompleteness in their technical arrangements, especially to the incompleteness of the controls, and these results must be confirmed before they can be accepted.

If we summarize this work we may say that the general results form an addition to our knowledge of the mechanism of anti-body reaction, although the mechanism of deflection itself remains obscure. What relation this reaction bears to specific anti-complement action or to the absorption of complement by any albuminous serum, or to mechanical precipitation is not clear. Before pronouncing final judgment upon the results described in this review, we must await the work of others in this field, for the number of factors entering into each experiment increases the chances of error in technique and in judgment to an extent that can only be controlled by an abundance of evidence. This is particularly true of the class of experiments in which the serum is obtained from animals immunized by inoculation with infected organs, for here the amount of infecting material must be slight compared to that of organ material inoculated, and therefore there is great danger lest the

[5] Leuchs, J.: *Berl. klin. Wchnsch.* (1907) 44, 68 and 107, has replied to Moreschi's criticism and contends that the deflection method is exceptionally accurate, delicate and specific in diagnosing typhoid fever from other bacteria such as paratyphoid.

organ-antibodies obscure the phenomenon due to any existing infection-antibodies. Of course any experimental evidence, either for or against, must be reënforced with all of the numerous controls demanded, or must prove the uselessness of these controls.

It is quite possible that these studies will throw some light upon the nature of complement. The use of the method outlined above for ordinary clinical diagnosis is evidently out of the question at the present time because of the special training required, but if the results above described are confirmed, it may well furnish a means for aiding in the discovery of yet unknown infectious agents, and in diagnosis, when employed by suitably trained specialists.

Finally, we may refer once more to the interesting results obtained by applying this method to the study of the pathologic physiology of tuberculosis and of syphilis.

That the technique is a difficult and complicated one has been pointed out with sufficient emphasis. It remains to investigate critically the constancy and accuracy of the method and to remove or mitigate sources of error.

In concluding I wish to refer to one other suggestion made by Wassermann and Bruck(35) to the effect that the softening occurring in a tuberculous focus is brought about by the enzyme-like action of complement which is bound in the diseased tissues by the recurring union of tuberculin and anti-tuberculin. They think that the complement comes from both the broken down leucocytes and from the infiltrating small round cells. They attribute the fever partly to a nonspecific effect such as follows the injection of any bacterial preparation and partly to the specific action upon the tuberculous tissue of material derived from the bacilli. However, another possibility suggests itself. We know that complement is blocked in the union of tuberculin and anti-tuberculin, and on the other hand we must suppose that complement has some definite function to perform in the healthy body, probably some function having to do with metabolism. Now it seems reasonable to suppose that the removal of complement in normal function must upset the physiological processes occurring in the body. This may well be true even when the binding of complement occurs locally as in an isolated tuberculous focus, but in the reaction to a general infection, when bacterial substance and anti-substance are being bound in widely scattered parts of the body, or in the circulation, an enormous amount of complement may be blocked. It will be important to determine how much complement is so blocked during infections, whether definite complements are blocked by certain bacteria and whether there is any relation between the symptoms and the loss of complement.

It was recently found by Pfeiffer(30), that the loss of available complement in the living body interferes with bacteriolysis.

II. THE AGGRESSIN HYPOTHESIS.

Bail's studies in infection and immunity convinced him that bacteriolysis has little or nothing to do with true immunity against disease and that Ehrlich and his school have followed the wrong clue. He brings forward the following facts in support of this contention:

(*a*) A rabbit is susceptible to anthrax, although its serum is lytic for the germ, while the naturally immune fowl has a serum which is not lytic.[6]

(*b*) In rabbits immunized against anthrax, and in those passively immunized, there is no bacteriolytic power. Bacteria disappear gradually as the result of the phagocytic action of cells, chiefly marrow cells, but do not disappear suddenly because of lysis.

Sobernheim found that animals upon which he conferred a high immunity against anthrax exhibited no agglutinating action and no lytic action, whereas his guinea pigs, immunized with the anthrax bacilli which had been grown at high temperatures or killed, exhibited no true immunity, but a rich content in immune bodies, the richest anti-body serums, however, affording no true immunity. Bail found similar but not identical, relations to hold with typhoid.

(*c*) A comparison of the sera of sheep, rabbits and cattle shows great variations in the amount of immune bodies contained, while these animals are nearly equally susceptible to anthrax.

(*d*) In test-tube experiments, a bacteriolytic serum is blocked when the conditions are approximated to those in the body by adding body cells to the fluid.

(*e*) Evidence is furnished (Hoke) that what has been said of anthrax holds for other organisms.

(*f*) Bail concluded from his studies that animals which survive the Pfeiffer test owe their lives not to bacteriolysis, but to active phagocytosis. He considers that the virulence of bacteria depends not upon toxin production, but upon the power of the bacteria to multiply in the infected body. He shows that after intravenous inoculations of animals, one with anthrax, the other with hay bacillus, the early reactions are the same in the two animals, the difference appearing only when anthrax begins to multiply, and even very shortly before death the organs of the anthrax animal are sterile.

He then seeks to explain the fact that a very small number of pathogenic bacteria may manage to obtain a foothold in the infected body and survive the attacks of the agencies protecting their host. He assumes that the protective body-forces are interfered with in some way, at first

[6] For other examples of this condition see Deutsch and Feistmantel.

locally and then generally, by certain obscure, hypothetical substances which he calls "aggressins."

He states that these substances, which he occasionally refers to as simple manifestations of energy, are minute particles "of a special kind" thrown off or secreted by living, uninjured bacteria. These particles do not come from solution of the bacteria, nor are they extracts of bacteria; they are thrown off as the result of irritation, which, he claims, is a very different process. He emphasizes particularly and repeatedly the importance of having living and uninjured bacteria in order to obtain aggressins. The aggressins are capable of promoting infection; they may be *preformed* in the bacterium, but they are *active* only in the infected body. They are contained in the infectious exudates, such as serous exudates and inflammatory œdemas, and may be recovered by centrifugalization and sterilization at low temperature, being found then in the fluid part of the exudate. The substances are different from anything hitherto recognized, and their peculiarities are that they promote the development of an infection, and that they interfere with the action of the protective body-forces of the infected host, particularly, if not solely by inhibiting phagocytosis.

The properties of aggressin may be grouped together as follows:

1. Sterilized aggressin added to nonlethal doses of the corresponding bacillus makes these doses fatal. Thus sterilized typhoid aggressin added to a nonfatal dose of typhoid bacilli and inoculated, causes death. This action is apparently a stimulation of the bacteria so that they produce toxins. Apparently he does not distinguish between promotion of infection due to stimulation of the bacteria, and that due to inhibition of the protective mechanism of the host.

2. Fatal doses of bacteria act more severely and acutely upon the addition of aggressin.

3. Inoculations of aggressins into the peritoneal cavity suspend the action of a bacteriolytic serum introduced at the same time.

4. Inoculations of aggressin confer immunity which is entirely different from bactericidal immunity.

5. Heating for one-half hour to a temperature between 55° and 60° destroys aggressin, sterilization with chloroform, toluol, or dilute carbolic acid weakens it, and the centrifugated aggressin exudate is to be sterilized by heating to 44° in order to preserve it for future use.

6. Injections of aggressin alone are only slowly poisonous, and never acutely fatal.

7. A fatal dose produces a prolonged illness, with emaciation preceding death.

8. Not all exudates contain aggressin, and it varies considerably in quantity in different exudates, which otherwise appear identical.

9. The aggressin is usually most abundant in exudates which are rich in cells.

10. Aggressins vary according to their age and mode of production, and it is possible, by means of serial inoculations, to increase the aggressive action of successive exudates very considerably, although a point is finally reached at which the series may suddenly terminate.

11. Aggressins with bacteria block phagocytosis—that is, they are negatively chemiotactic—but aggressins alone act very slightly.

Basing his classification upon the power to produce aggressins, Bail divided bacteria into:

(*a*) True parasites which always produce aggressins; (*b*) half parasites, the aggressin power of which is very variable; (*c*) saprophytes.

The body may develop bactericidal immunity against the half parasites, but not against true parasites. As types of true parasites, he gives anthrax and chicken cholera, germs the aggressive action of which is unfailing. Artificial extracts of these germs have no aggressive action. Most epidemic diseases are produced by half parasites, as types of which he gives typhoid, cholera, dysentery, and plague. The toxicity of the half parasites is often extremely high.

The toxicity of a germ has nothing to do with aggressivity, and extremely toxic bacteria may be half parasites: the class depends upon the capacity of the germ "to infect under all conditions the susceptible living creature from its own natural habitat; that is, the animal that has succumbed." True parasites readily furnish an immunity by the aggressin method, but their extracts do not even confer a heightened resistance. Half parasites vary in their power to produce aggressins and to confer an anti-aggressive immunity.

There have been numerous objections to the claims made by Bail, and a series of articles has been published on this subject from different laboratories while Bail and his pupils have undertaken to support and strengthen the "aggressin doctrine" as Bail names his hypothesis. Pfeiffer and Friedberger(8) have shown that Bail's attempt to explain the blocking of the bacteriolytic action of a serum as due to aggressins is not tenable.

Wassermann and Citron(11) dispute Bail's claim that he is dealing with a new substance never before found outside of the infected body. They obtained aggressins (*a*) by growing bacteria in sterile exudates in test tubes; (*b*) by growing bacteria in sterile normal rabbit serum in test tubes, and (*c*) by making aqueous extracts of bacteria. They concluded that Bail had nothing new, but was dealing with dissolved bacterial substances. However, Citron(4) in a later article, notes that there are differences between the extracts prepared by different procedures, and believes that according to present evidence it is probable that the most effective aggressins can be extracted only from living bacteria.

Bouchard, as long ago as 1891, obtained typical aggressin actions by inoculating soluble bacterial products, together with the bacteria.

Strong(10) by using aqueous extracts of plague, obtained a mild immunity in monkeys which, however, was not demonstrable in guinea pigs. This is of particular importance from the fact that plague immunity is known to be non-bacteriolytic immunity, and Bail states repeatedly that non-bacteriolytic immunity is characteristic of aggressins

Doerr(5) also thinks that Bail is dealing with dissolved bacterial substances, as he obtained the precipitin reaction with aggressive exudates, and he brings forward criticism against the work of Bail, on the score of the inaccuracy of the so-called sublethal doses. He also found that aggressins are of themselves injurious, and that one aggressin promotes infection with a different species of bacillus.

Levy and Fornet(7) were able to demonstrate the aggressive nature of filtrates of 24- to 48-hour bouillon cultures of typhoid and paratyphoid bacilli. They found that these filtrates were "infection-promoting" to the extent of increasing fivefold the virulence of typhoid bacilli. The addition of filtrate or exudate aggressin to leucocytes blocked the phagocytic power against typhoid bacilli, which was otherwise present.[1]

Ballner(3) found that nonbacterial exudates obtained from guinea pigs increased the infectious action of Friedländer's bacillus in rabbits, in other words exercised an aggressive action. He could not obtain an anti-aggressin immunity with this germ.

Wolff-Eisner(13) reviews the aggressin literature at length and concludes that the aggressins are nothing but endotoxins from bacteria; that they alone are not present in sufficient amount to act strongly, but that, upon addition of fresh bacteria, a summation effect is obtained and the animal dies quickly. He thinks this also explains the negative chemiotaxis occurring with aggressins.

What part the aggressin plays in the blocking of leucocytosis is also in dispute. Citron, in studying meningococcus found that there was no relationship between aggressivity and power to block phagocytosis, while Salus' work raises the question as to whether the aggressin action is anti-chemiotactic at all, as the aggressin acts even though it is injected in a different part of the body from the bacteria.

On the other hand, Bail and his school have published a series of articles dealing with the aggressins in cholera, typhoid, dysentery, plague, tuberculosis, *Bacillus subtilis,* chicken cholera, hog cholera, pneumococcus and staphylococcus.

Bail has satisfied himself that aggressin action occurs in tuberculosis also, although in this case active phagocytosis continued after addition of aggressins. Koch long ago obtained the same action by the use of dead cultures, thus ruling out any vital action in the production of aggressins.

The last article from Bail is a lengthy rejoinder to the criticism of Wassermann and Citron. He contends that the extracts used by Wassermann and Citron are altogether different from aggressins, and that

[1] Concerning Bail's statement that the aggressive property of body fluids is due to secretion products from bacteria, see v. Pirquet and Shick, "Die Serumkrankheit." Wien, 1905.

the various properties which they find in these extracts in no way alter the significance of the properties that he has attributed to aggressins. The points of difference between the "natural aggressin" obtained from infected animals by Bail's method, and the "artificial aggressins" obtained by the various extractive procedures are discussed at length.

1. In the case of cholera, natural aggressins promote the infection, but do not destroy or stop lysis of the spirillum, nor cause loss of complement even when tested by the deflection test, the complement being present not only in the infected body but also in the aggressin exudate itself; whereas the artificial aggressin blocks lysis strongly and promotes infection by this means.

2. Similarly, when aggressin and a specific serum are inoculated into the peritoneal cavity of a guinea pig they do not block lysis, whereas the artificial aggressin with a specific serum does so.

3. Aqueous extracts of cholera and typhoid are so full of bacterial particles that they furnish a precipitate even in the presence of a normal serum; while natural aggressins may altogether fail to precipitate, even in the presence of a strong specific serum. The artificial aggressins do not occur in the course of natural infections, and hence are altogether removed from comparison with natural aggressins.

However, after disputing virulently the contention of Wassermann and Citron that Bail is dealing with extracts of bacterial substance, the latter makes certain concessions. He states that shaking bacteria in distilled water injures the bacteria. The extracts therefore do not fulfill the requirements of aggressins as defined by Bail, but he adds "although we acknowledge that some bacteria have loosely separated aggressin easily shaken off and to be obtained in small amounts." Again, "it is not impossible that aggressin preëxisting in the animal body may be recovered in small amounts *extra corpus*;" and he finally expresses a belief that some of Citron's artificial aggressins obtained from living bacteria contained small amounts of natural aggressin intermixed. Again, he states that not every exudate is aggressive, and not every aggressive exudate evidences pure aggressivity. In addition to the aggressive substances—if there are such—there may be present in an exudate or œdema "ordinary bacterial substances which are the original artificial aggressins of Wassermann and Citron and it is these latter which block hæmolysis."

He also states with regard to the solution of bacterial substances that in experiments with typhoid he almost always obtained aggressins in his exudates, but could prove by the method of complement deflection that ordinary bacterial particles were not in the exudate. The indications are that the aggressivity of exudates is in inverse ratio to the power to deflect complement. He holds that complement deflection is

due to bacterial particles causing precipitation. No essential solution of bacterial substance, then, occurs in the animals, which fact agrees, he thinks, with the one that typhoid bacilli after inoculation rapidly acquire a resistance to bacteriolysis. However, with cholera, the case is different, the exudate containing dissolved bacterial substance in solution.

"The conclusion is evident that it depends upon the course of an infection whether an animal has in its exudate larger or smaller amounts of dissolved bacterial substance."

The smaller the amount of dissolved bacterial substance in an exudate, as determined by complement deflection, the stronger is the aggressive action of the exudate.

These statements indicate a distinct recession from Bail's original position, for on the one hand he acknowledges that artificial bacterial extracts may contain aggressin and on the other, that aggressive exudates may contain in solution other bacterial substances together with aggressins.

Bail also discusses at length the relation between complement deflection and precipitation, particularly with regard to its bearing upon our understanding of aggressins. While artificial aggressins inhibit bacteriolysis, Bail notes that the third of a series of guinea pigs inoculated in turn with cholera, furnishes a natural aggressin which contains complement completing the action of anti-cholera serum. This complement action of the aggressin exudate is stronger in the third than in the second of a series of guinea pigs; and stronger in the second than in the first. This change is so regular that when it is absent it is safe to attribute it to an overdose of bacteria in setting the test.

In serial inoculations aggressivity increases until the danger arises that the series will cease from some cause not clearly understood. As the aggressivity increases, there is a decrease in the power of the exudate to block hæmolysis. Bail brings this forward in rebuttal of Citron's argument that the power to block hæmolysis furnishes an index of the aggressivity of the exudate. He discusses the phenomena of precipitation, complement deflection and multiplicity of complements. He agrees completely with Moreschi that deflection is not a function of the union of amboceptors with specific substances, but is due to gross or microscopic precipitation.

He states that he disregards the plurality of complement idea, which he thinks was overthrown by the discovery of complement deflection, and he agrees with Bordet in looking upon complement as a "single fermentative, complementative activity" of the body juices. However, he is not consistent in this position, for he finds that in some of his aggressin experiments the heart's blood of the animal contains hæmolytic

complements, "and usually bactericidal complement not only for cholera and typhoid, but also for anthrax." This is a tacit confession that different complements are needed in these different reactions.

He does not agree with Citron in attributing to natural aggressin the power of complement absorption, but he gives examples showing how natural aggressins may lead to the blocking of hæmolysis.

Bail considers that the leucocytes are the chief source of complement. He thinks that extracts of bacilli hold back leucocytes more than natural aggressins do. He believes that inoculation of extracts acts just as does the inoculation of larger amounts of bacteria to promote the growth of the inoculated bacteria so that these, by means of their newly acquired aggressivity, restrain the growth of leucocytes. This is rather a complicated mode of procedure. Aggressin alone has no power to bind leucocytes, but only acts in the presence of bacteria. This he can not explain, but he found qualitative differences. The addition of cholera aggressin causes death by intoxication with no leucocytosis in a guinea pig previously inoculated with cholera and anti-cholera serum, the action being unlike that following the addition of cholera extracts or of sterile bouillon. This he brings forward as an additional proof of the difference between artificial and natural aggressins.

Turning to the question of immunity against infections, Bail holds that anti-bacterial immunity is not a true immunity, and that this can be given only by creating "anti-aggressin." These anti-aggressins are distinctly different from anti-bacterial substances, for the anti-aggressin immunity is certainly not bactericidal immunity in the cases of anthrax, chicken cholera, swine plague, and plague, dysentery, capsulated bacillus, and typhoid; while in the case of cholera he has never succeeded in obtaining an anti-aggressin immunity which did not also exhibit a bacteriolytic immunity. The determinations in these cases were made both by test-tube experiments and by Pfeiffer tests. The anti-aggressin immunity is a phagocytic immunity, at least in the case of typhoid.

However, even with strong anti-aggressive immunity, the infecting bacteria may survive and multiply in the host, but they cause no symptoms. Citron could also verify this, finding virulent hog cholera bacilli in an immunized animal after five and one-half months. He contends not only that bactericidal immunity is not a true immunity, but that this bactericidal power can not be deduced from the power of the serum to block hæmolysis; and, further, he claims that Wassermann and Citon are wrong in regarding the presence of amboceptors in an inoculated animal as an index that the reaction of immunity has occurred in those cases in which the cholera germ is still capable of living somewhere in the body of the immunized individual.

Bail gives the occurrence of strong phagocytosis in spite of severe infection as a characteristic of anti-aggressin immunity.

There is a negative stage after the inoculation of aggressin during

which the animal exhibits marked hypersusceptibility to fresh inoculations of the germ. He also states that anti-aggressin immunity is one of the oldest methods of immunization, although its essentials were never before understood. He claims that the experiments of Wassermann, Ostertag and Citron with vaccination with suitably weakened bacilli, is nothing but a modified form of Pasteur's immunization, and adds: "We consider Pasteur immunity as the only true immunity, but it is nothing else than an aggressin immunity. This is shown by its not having a high content in anti-bodies."

A review of the work both for and against aggressins leaves it questionable whether Bail and his school have made any real contribution to bacteriology or immunity. It is by no means an easy matter, in many cases, to obtain a clear idea of their meaning, but some of the phenomena, which they describe as aggressive in nature, can hardly be due to any single cause and are probably to be explained by considering together a series of processes in the bacteria and another series in the infected host. Their claim that their aggressins are newly described substances has been nearly overthrown and most of the characteristics have been found under other conditions. As to the newness of anti-aggressin immunity, all doubt is set at rest by Bail's statement that it is the same as Pasteur's immunity.

The lessons to be learned from the aggressin work are not new; the same lessons are being taught by the workers upon opsonins and endotoxins, and they are:

1. That there are very great differences in activity between otherwise apparently identical strains of a species of bacterium; 2. That bacteria undergo some important alteration when transferred from a saprophytic to a parasitic existence; 3. That there are marked differences in the reactions occurring in various species of bacteria after they are inoculated into animals; 4. That the phenomena of agglutination, bacteriolysis or phagocytosis do not separately afford an explanation of anti-infectious immunity; 5. That the products of bacterial metabolism are numerous and differ among themselves, and that the products differ according to the pathogenicity of the bacterial strain.

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INFANT FEEDING AND ITS INFLUENCE UPON INFANT MORTALITY IN THE PHILIPPINE ISLANDS.[1]

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I. INTRODUCTION.

Infant mortality is the most serious, important and urgent problem in preventive medicine in the Philippine Islands. The following figures of births and deaths for the *City of Manila* are taken from the records of the Bureau of Health:

Year.	Births.	Deaths.	Deaths (under 1 year of age).
1903	3,387	9,394	3,872
1904	6,341	11,357	6,029
1905	7,779	9,731	4,676
1906	8,679	9,486	4,218
Total	26,186	39,958	18,795

[1] Read by abstract at the Fourth Annual Meeting of the Philippine Islands Medical Association, March 3, 1907.

The number 18,795, for the deaths of infants under 1 year of age, represents 47 per cent of the total mortality, and 71 per cent of the total recorded births.

No reliable figures are available from the provinces, but it is probable that the ratios will not be found materially to differ from the ones derived from the records in Manila, for whereas Manila has better sanitary conditions, and the services of hospitals, physicians and nurses are more regularly sought in the city, the provinces on the other hand have fresher and better milk and other foods, and infections are perhaps less frequent.

Three hundred and seven American children were born during the four years covered by these statistics, and while no accurate figures are available, the infant mortality among these was less than 5 per cent. Very similar results are obtained from statistics which one of us personally compiled, containing the record of 150 native children born to educated parents during the same period of time. However, in these two classes of patients rachitic tendencies, marasmus, anæmia and other damaging influences of malnutrition are sufficiently prevalent to prove that even in the absence of pure, fresh milk, we are not using the available foods to the best advantage.

On examining the recorded causes of death a little more closely we find some interesting and instructive figures regarding the death of 18,795 infants in Manila during the last four years. In 10,484 instances the cause of death is given as convulsions; in 1,416 (for three years only) diarrhœal diseases and dysentery; and in 780 (for three years only) simple meningitis is credited with the fatal result. In addition to these figures large numbers of certificates of death where the cause is given as tetanus, lack of care, debility, etc., are recorded. We but confirm the expressed opinion of Major E. C. Carter, formerly Commissioner of Health for the Philippine Islands, and many other prominent health officials and physicians, in stating that an overwhelming percentage of the 10,484 deaths reported as due to convulsions were in reality caused by gastro-intestinal diseases, the result of dietetic errors; this number may also safely be increased to include most of the cases of so-called tetanus, meningitis, debility, etc. Tetanus is prevalent in the Philippine Islands and it is to be expected in a certain number of babies because of the lack of care in treating the cord at birth, but in six patients which one of us was able to see during life, and in three more where Musgrave made post-mortem studies, the spasms were of other etiology and tetanus was not present.

Rickets and marasmus are not mentioned in the recorded causes of death, but both diseases are present among foreign and native children. We are convinced after a careful study of the records, the conditions and our own observations, that more than 75 per cent of the deaths of babies in Manila are primarily due to dietetic errors.

Major E. C. Carter, formerly Commissioner of Public Health, makes the following statement in his annual report for 1903:

> This excessive infant mortality is one common to all tropical countries. In Manila it appears chiefly to depend upon ignorance with respect to the proper care and feeding of young children and the difficulties of obtaining suitable food where nursing by the mother is for any reason impracticable or the supply of breast milk is insufficient. Fresh milk is almost impossible to obtain, and when obtained is usually of poor quality and contaminated by improper handling. In the absence of ice its preservation is practically an imposibility and no attempt is made to modify its constitution so as to conform more nearly in character to human breast milk. The destructive epidemics of rinderpest have also largely destroyed the few milch cattle formerly in the Islands and there has been but little resort to goats as a source of milk supply. The so-called Australian milk is costly, its use is not general and it is not well borne by many. The employment of prepared infant foods is understood by but few, and their cost places them beyond the reach of the poorer classes. The same applies to the use of condensed milk, which is at present the most available source of supply of food for infants. When used it is frequently improperly diluted or contaminated by the use of water from an impure source, giving rise to intestinal disorders and malnutrition which are rapidly fatal.

Major Carter in his annual report for 1904 again emphasized the statements given in his report for 1903 and in addition points to the invasion of the Islands by the "germ infected nursing bottle," he calls attention to the use of the milk of the coconut in feeding, and he started a campaign of education by distributing broadcast a bulletin on the care of children, which was prepared by a committee of native physicians.

Dr. V. G. Heiser, at present Director of the Bureau of Health, in his annual report for 1906 states that as a result of this bulletin the consumption of milk has increased by probably 500 per cent, nearly all the output being used as food for infants, and he further points out that notwithstanding this fact, there has been no appreciable decrease in infant mortality and he considers this to be due to the improper care and handling of both the milk and its containers. Dr. Heiser states that probably 95 per cent of the milk used is from the carabao.

However, even the large infant mortality, disastrous as it is, does not tell us of the pernicious influences brought about by the conditions which produce this mortality, upon those who escape death in infancy. A large percentage additional to the 71 per cent of infants who die before the end of their first year, is to be credited to those who are left with crippled constitutions and who later become unnecessarily susceptible to other diseases. This supplementary mortality must be charged to the same lack of care of the helpless ones, which makes the loss of so many infants possible.

The problem of infant mortality and infant feeding is, of course, a fundamental one in all parts of the world and it is particularly so in cities, but here it is even more complex than it is in other places because of at least two important reasons—one, the almost complete absence of

good, fresh milk, and the other, the lack of satisfactory literature bearing upon the subject. So far as we are aware, there is not a book or exhaustive article which deals with the problem of infant feeding in countries where a supply of fresh milk is lacking and where, in addition, the ability of mothers to nurse their offspring is reduced to a minimum for reasons which we will discuss below.

II. HABITS AND CUSTOMS OF THE PEOPLE.

A. THE NATIVE MOTHER.

The habits and customs of the people deserve a passing notice if we consider that the feeding of the child begins with conception. A parturient native woman is generally a happy one, proud of her condition, and she as a rule continues her regular habits and vocation during the period of her gestation. The diet during this time is of the usual variety, which contains an excess of carbohydrates.

Confinement, particularly among the poorer class of people, is of a very primitive type. In Manila, over 50 per cent of the children are born without medical attendance, usually with the aid of a midwife whose presence often does more harm than good. Mechanical assistance is afforded to the mother by passing a rope or folded sheet around the body just above the fundus, whereupon one or more friends pull upon the ends. The bad results to both mother and child following this and many other even more dangerous procedures, need no discussion here.

B. THE NATIVE CHILD.

The native child usually has the best attention which its mother can afford and which she knows how to administer, but the density of the ignorance and even of the superstition which exists among the uneducated classes is remarkable, and in addition, generations of self-medication have resulted in the extensive adoption of customs which are of the most pernicious type, often maintained with a persistence which seems culpable and vicious in the face of gratuitous enlightenment.

Breast feeding is probably attempted in almost every case, but the percentage of exclusively breast-fed children is certainly much smaller than it is in many other countries. This is due to several causes among which may be mentioned infections, injuries to the mother at childbirth and, most important of all, the lack of sufficient and proper food for the mother during the puerperum; we also must remember that the hereditary influences of generations of artificial feeding are always present to contend with. The average Filipino woman is poorly developed, and even those who have borne several children usually have small breasts, so that the milk-giving capacity is at a minimum. The conditions which have been outlined and many others, bring about the necessity of instituting artificial food for breast milk in infant feeding to an extent, and at an

age of the infant, probably not surpassed if it is equaled in any other country.

Mixed feeding is usually the first departure from exclusive breast feeding; it is instituted early and continued as long as milk may be obtained from the breast, or until long after the child should be weaned. The only contraindication to breast feeding among the poorer classes is the lack of milk; no cause for discontinuation being found in tuberculosis, in other infectious diseases or in pregnancy. The accessory articles of diet in mixed feeding are very numerous, and the methods of preparation and administration primitive, but as they are identical with the ones administered in pure artificial feeding, their consideration will be postponed until that heading is reached.

Artificial feeding is rarely resorted to entirely so long as the breast milk continues, but in most of the instances of mixed feeding the nourishment which is taken is mainly from artificial sources, which will now be discussed in detail.

Milk is the most important of the articles of diet. That of cows, goats, and carabaos is used and a large assortment of canned and condensed milks is also employed. Other prepared foods of foreign manufacture are given to a limited extend in addition to the different milks, and homemade preparations in large variety make up the bulk of the infant food among the poor people. Most of the latter articles are mixtures of starch and sugar, prepared without proper regard to cleanliness, and among these may be mentioned the rice sticks, made by boiling rice and sugar until a glue is formed, which can be molded into a stick to be sucked by the child. Potatoes, bananas and other fruits are given at a very early age, and meat feeding is very frequently instituted before the eruption of the temporary teeth. It is not an infrequent occurrence at autopsies to find pieces of undigested meat in the stomachs of four months' old children. Not only does the quality of the foods and their indiscriminate use, regardless of the age of the child, bring disaster, but the character and percentage of the diluents also contribute very much to the bad results. Throughout the sad story—and this is the pity of it—nothing but the ignorance of the people is to blame for the results.

C. THE FOREIGN MOTHER AND CHILD.

In Manila the social customs are such that in general the foreign woman neither cares so well for herself nor does she make as good a mother as she would in her home country. Nevertheless, the children of foreigners and of the educated class of Filipinos thrive, although surrounded by the same climatic and other unavoidable evils which encompass those of the ignorant classes. The infant mortality among foreigners and wealthy natives compares favorably with that in other lands; the children are fairly strong and not overburdened with the diseases of malnutrition so common in all countries.

III. A STUDY OF THE CONDITIONS.

A very complex condition appears before us for study, to judge from the preceding brief and incomplete résumé of facts. However, the limits of this paper will allow of the consideration of but one of the problems, namely, that of infant feeding, and in discussing this topic we will first take up a consideration of the available materials.

THE AVAILABLE FOOD SUPPLY.

Milk is the first of the articles to be considered and it may be classified as either fresh or preserved. Among the fresh milks we will consider human, cows', carabaos' and goats' milk and among the preserved varieties we have many brands of the sterilized, condensed and malted type.

(a) HUMAN MILK.

The percentage of American mothers who are able to nurse their children in Manila is higher than it is in general in American cities. The quality of the milk is of a very good average, perhaps with a tendency to a high sugar index, with a correspondingly lowered proteid and fat content, as is shown in the following table:

TABLE NO. 1.—*Analyses of ten samples of breast milk from American women who have infants from 20 days to 2 months old.*

No.	Specific gravity.	Water.	Solids.	Ash.	Fat.	Sugar.	Proteid.
1	1.032	88.80	11.20	0.20	2.40	6.10	2.50
2	1.030	87.19	12.81	.11	5.55	6.07	1.08
3	1.029	88.74	11.26	.33	3.48	6.31	1.14
4	1.030	86.80	13.20	.14	4.44	7.58	1.04
5	1.027	84.47	15.53	.11	7.27	7.16	.99
6	1.027	84.44	15.56	.25	6.36	6.98	1.97
7	1.033	89.45	10.55	.26	1.90	6.81	1.58
8	1.030	87.22	12.78	.27	5.48	6.23	1.42
9	1.029	88.62	11.38	.34	3.61	6.28	1.18
10	1.032	89.41	10.59	.23	1.92	6.78	1.60
Average	1.0299	87.46	12.48	.22	4.24	6.63	1.45

The analyses of breast milk among the better class of Filipino women who can and do partake of a liberal diet and who otherwise obey the mandates of hygiene also gives a good average, as shown in Table No. 2.

TABLE No. 2.—*Analyses of breast milk taken from the wealthier class of Filipino women.*

No.	Specific gravity.	Water.	Solids.	Ash.	Fat.	Sugar.	Proteid.
1	1.030	86.22	13.78	0.27	5.78	6.33	1.40
2	1.031	86.78	13.22	.17	4.34	7.76	.95
3	1.027	84.43	15.57	.26	6.34	6.98	1.97
4	1.029	85.49	14.51	.11	6.64	6.07	1.69
5	1.028	88.17	11.83	.41	3.35	5.91	2.16
6	1.030	88.30	11.70	.23	3.21	7.18	1.08
7	1.031	88.82	11.18	.12	2.61	7.59	.92
Average	1.029	86.88	13.11	.22	5.38	6.83	1.45

However, a study of the breast milk among the poor people gives some interesting figures. In the first place, the quantity is small and the period of active lactation short. Analyses of ten samples of milk show a persistent high specific gravity, high sugar index, with low proteid and fat. This is apparent from the following table:

TABLE No. 3.—*Analyses of ten specimens of breast milk from native women of the poorer classes, with infants from 10 days to 1 month old.*

No.	Specific gravity.	Water.	Solids.	Ash.	Fat.	Sugar.	Proteid.
1	1.035	86.83	13.17	0.11	2.84	8.70	1.52
2	1.038	87.29	12.71	.34	2.55	8.29	1.53
3	1.034	86.91	13.09	.15	2.33	9.20	1.41
4	1.036	87.43	12.57	.13	2.98	8.08	1.38
5	1.030	87.20	12.80	.11	3.58	7.11	1.40
6	1.030	86.60	13.40	.14	4.50	7.62	1.14
7	1.030	86.71	13.29	.15	4.02	7.98	1.14
8	1.030	88.04	11.96	.09	2.67	8.14	1.02
9	1.030	86.96	13.04	.16	3.97	7.83	1.08
10	1.031	87.97	12.03	.15	1.31	6.87	1.31
Average	1.033	87.19	12.81	.15	3.07	7.98	1.29

A study of these analyses shows that even in breast feeding in Manila there are unusual problems to be met. In order fully to appreciate this fact we have taken the averages from the preceding tables and placed them in the following one, which also gives average human milk analyses from two representative sources, for comparative purposes.

TABLE No. 4.—*Showing comparison between human milk analyzed by several authors and the findings in Manila.*

Source.	Fat.	Sugar.	Total proteid.	Casein.	Whey proteid.
Averages given by Rotch	3.00–4.00	6.00–7.00	1.00–2.00	0.59	1.23
Averages given by König	3.80	6.20	2.30	1.00	1.30
Average from American women in Manila	4.24	6.63	1.45		
Average from Filipino women in Manila of—					
Better class	5.38	6.83	1.45		
Poor class	3.07	7.98	1.29		

Some of the discrepancies between the analyses of human milks from women of the Tropics and of those given for other countries are usually explained by the difference in diet, and this also partially makes clear the variations due to the racial differences in women living in the Philippine Islands. However, there are other influences such as heredity, nervous temperament, climate, etc., which here play an active part and which must not only be reckoned with in determining what is abnormal in the mother's milk, but also in *fixing standards of normality* for the infant's requirements with reference to nutrition. For example, according to our standards the high sugar index and the low fat content found in the breast milk of the native women of the lower classes are too far from the normal to accord with our present conception of the physiology of nutrition of the infant and, according to the same standards, they are partly responsible for the gastro-intestinal disturbances and for some of the malnutrition and lack of development of the children of these classes.

However, it is not at all certain but that our standards of averages may need some adjustment in this respect, and it may be true that the child of parentage which for generations has lived in the Tropics may demand more sugar and less fat than we have been accustomed to recognize as normal.

(*b*) OTHER FRESH MILKS.

1. Fresh cows' milk, because of the dearth of horned animals, due to rinderpest, is very difficult to obtain in any considerable quantity and its price is, and for some years it must remain, prohibitive for most of the people. Adulteration of the available cows' milk is exceedingly common and flagrant; the adulterants consist of carabaos' or goats' milk, canned milks, and often of chalk, limewater and other substances. Bacteriological examinations show this milk to be unfit for use. After repeated efforts we were unable to obtain ten samples from the market in order to submit a table of comparative results.

Examinations of ten samples of fresh cows' milk from the Bureau of Agriculture in Manila are given below. These animals are well selected and are specially cared for by Government officials.

TABLE No. 5.—*Analyses of ten samples of cows' milk from stall-fed animals, the property of the Bureau of Agriculture in Manila.*

No.	Specific gravity.	Water.	Solids.	Ash.	Fat.	Sugar.	Proteid.
1	1.034	89.78	10.22	0.72	3.73	2.39	3.38
2	1.032	89.90	10.10	.63	2.63	4.36	2.48
3	1.035	88.22	11.78	.65	3.44	4.57	3.12
4	1.033	89.50	10.50	.60	2.09	5.07	2.74
5	1.031	89.55	10.45	.75	2.52	3.87	3.31
6	1.032	89.22	10.78	.71	2.42	4.40	3.25
7	1.033	90.59	9.41	.65	1.64	4.00	3.12
8	1.028	87.97	12.03	.65	4.34	4.11	2.93
9	1.034	86.38	13.62	.70	3.73	4.86	4.33
10	1.032	89.80	10.20	.60	1.66	5.07	2.87
Average	1.032	89.09	10.91	.66	2.82	4.21	3.15

In the following table the averages from the preceding ones are compared with those given for fresh cows' milk by two distinguished authors:

TABLE No. 6.—*Showing comparison between the results of examinations of cows' milk as given by other authors and as determined in Manila.*

	Fat.	Sugar.	Total proteid.	Casein.	Lact-albumin.
Average fresh cows' milk (König)	3.70	4.90	3.50	3.00	0.50
Average fresh cows' milk (Rotch)	4.00	4.75	3.50	2.66	.84
Average fresh cows' milk Manila	2.82	4.21	3.15		

The contents of fresh cows' milk varies between very wide limits in all parts of the world, but in Manila this variation is excessive and is in part due to the alteration in the kind of food to which the cows have been accustomed, to the difference in the care of the animals and to difficulty of securing *average* milks because of the lack of large herds of cattle. As it is impossible to obtain an average, it is necessary to examine the milk from each animal or herd before it can intelligently be modified for infants' use, and even after these precautions have been taken many of these milks are of a composition which renders proper modification very difficult. The worst cases of rickets to be seen in the Philippine Islands are often observed among children who are fed upon so-called fresh, cows' milk. The average bacterial count in five samples of milk bought in the market was 2,160,000 and the average from five samples from cows from private families gave 765,000. As a result of personal observation regarding the care given to milk, animals, vessels and the surroundings

of the stables in general, we can not recommend the use of unboiled, fresh milk in Manila obtainable in the open market for human food, and until conditions are much improved, its use as food for infants seems almost criminal.

2. Goats' milk is to some extent employed in Manila as an infant food, but the supply has been limited, and it is very dirty and of poor quality as it is put on the market. The quality is shown by the following table:

TABLE No. 7.—*Showing the results of the examination of eight samples of ordinary goats' milk in Manila.*

No.	Specific gravity.	Water.	Solids.	Ash.	Fat.	Sugar.	Proteid.
1	1.032	85.69	14.31	1.97	5.18	3.66	3.50
2	1.030	84.11	15.89	1.82	6.56	4.13	3.38
3	1.035	84.76	15.24	2.07	4.95	4.01	4.21
4	1.036	86.66	13.34	2.07	3.04	3.77	4.46
5	1.034	82.39	17.61	2.45	7.73	2.39	5.04
6	1.034	85.48	14.52	2.00	5.01	3.81	3.70
7	1.035	80.20	19.80	1.75	8.95	5.53	3.57
8	1.030	88.03	11.97	2.02	4.41	1.02	4.52
Average	1.033	84.66	15.33	2.02	5.73	3.54	4.05

The Government has recently imported some milch goats from Malta and if suitable food is available and conditions are otherwise found to be satisfactory for the propagation of these animals, this importation will result in doing much good. The reaction of the changed environment upon these animals is still problematical and a study of the milk to be obtained from them after acclimatization remains to be made. Analyses of seven samples of milk from this herd after the animals had been two months in Manila are given in the following table:

TABLE No. 8.—*Showing the result of the examination of seven samples of goats' milk from a herd of Maltese goats imported by the Government.*

No.	Specific gravity.	Water.	Solids	Ash.	Fat.	Sugar.	Proteid.
1	1.028	87.97	12.03	0.63	4.78	3.31	3.31
2	1.029	87.39	12.61	.67	4.29	4.34	3.31
3	1.031	86.96	13.04	.59	4.83	4.34	3.38
4	1.030	87.57	12.44	.79	4.57	3.45	3.63
5	1.032	87.97	12.03	.63	3.24	5.87	2.29
6	1.030	84.90	15.10	.60	6.66	4.40	3.44
7	1.030	86.97	12.03	.59	4.88	4.31	3.25
Average	1.029	87.10	12.90	.64	4.73	4.27	3.23

Averages from the two preceding tables, compared with those of goats' milk given by one American and one European author, are placed in the following table:

TABLE No. 9.—*Showing comparison between results of the examination of goats' milk as given by other authors and as determined in Manila.*

Kind of animal.	Fat.	Sugar.	Total proteids.	Casein.	Lact-albumin.
American goats (Rotch)	4.30	4.00	4.70		
European goats (König)	4.80	4.40	4.30	3.20	1.10
Maltese goats in Manila	4.75	4.27	3.23		
Native goats in Manila	5.73	3.54	4.05		

The same objections as those already mentioned for cows' milk must obtain until the general conditions for securing and caring for this milk have been much improved. All of these milks as they appear on the open market are exceedingly dangerous bacteriologically, and the lack of large herds makes it impossible to obtain any quantity of *average, mixed milk*.

3. Carabaos' milk is extensively used as an infant food among the poorer people and it is the least adapted to this purpose of any which we have as yet studied. The results of analyses of 6 samples of carabaos' milk made by Charles L. Bliss, formerly of the Chemical Laboratory, Bureau of Science, are given in the following table:

TABLE No. 10.—*Showing results of analyses of carabao milks.*

	1.	2.	3.	4.	5.	6.	Averages.
Age of animal	15 yrs.	13 yrs.	6 yrs.	8 yrs.	16 yrs.	10 yrs.	
Age of calf	3 mos.	2 mos.	2 yrs.	1 yr.	4 mos.	7 mos.	
Amount of milk	1,700	1,550			1,000	1,500	
Specific gravity	1.040	1.037	1.032	1.032	1.038	1.039	1.036+
Fat	12.76	9.55	13.22	11.56	8.65	8.36	10.63
Sugar	3.62	3.82	3.34	2.90	4.19	4.50	3.73
Proteid	6.97	6.75	6.78	6.34	5.54	5.46	6.31
Ash	.99	.09	.90	.82	.85	.85	.88
Total	24.34	20.02	24.24	21.62	19.23	19.17	21.44
Solids by evaporation	25.28	20.83	24.24	22.52	19.92	19.79	22.09
Water	74.72	79.17	75.76	77.48	80.08	80.21	77.90
Solids not fat	12.52	11.28	11.02	10.96	11.27	11.43	11.41

Two samples, 3 and 4, were treated with dilute hydrochloric acid. The coagulum found was compared with that produced in fresh cows' milk similarly treated. To 10 cubic centimeters of each of these milks 5 drops of hydrochloric acid of 1.12 specific gravity were added and the whole heated to 37–38° C. Both carabao milks became solid immediately. The coagulum very closely resembled that produced by rennet in cows' milk. The result with the cows' milk was negative. This would indicate that carabao milk would need to be diluted considerably for infants' feeding, as it would coagulate.

Carabaos' milk as it is obtained and marketed in Manila, is about as dangerous and dirty a mixture as it is possible to have. Bacteriologically, it is excessively contaminated and chemically it is not easy properly to modify for the use of infants.

(c) PRESERVED MILKS.

A great variety of these are imported into Manila, and in enormous quantities. The records of the Bureau of Customs show that 4,041,703 pounds of condensed milk, with an approximate value of ₱800,000 and 59,809 gallons of fresh milk, with an approximate value of ₱147,000 were imported into Manila during the year 1906.

The following Table No. 11 shows the principal brands on the market, with the results of the analyses of samples, each obtained in the open market:

TABLE No. 11.—*Showing results of analyses of samples obtained in the open market of some of the most generally used preserved milks in Manila.*[a]

Name.	Specific gravity.	Water.	Solids.	Ash.	Fat.	Sugar.	Proteid.	Remarks.
Bear milk	1.029	87.87	12.13	0.67	4.27	4.06	3.07	Average from 3 samples. Sterile. No concentration; no adulterants.
Dragon milk	1.029	87.66	12.33	.76	4.12	4.35	3.11	Do.
Weribest milk	1.032	88.20	11.20	.71	3.24	4.75	3.10	Sterile; no concentration; no adulterants.
Highland evaporated cream.	[b]1.077	70.61	29.38	1.80	7.86	11.13	8.40	Average of 3 samples. Sterile; concentrated; no adulterants.
Bear concentrated.	[b]1.040	70.95	29.05	1.75	9.67	9.79	7.84	Sterile; concentrated; no adulterants.
Bear cream[c]	.943	55.95	44.09	.46	38.07	3.22	2.29	Average from 2 samples. Sterile; slightly concentrated; no adulterants.
Australian	[b]1.045	60.85	39.15	2.32	14.00	13.52	9.31	Cold storage. Concentrated. Contained a compound of boron. 3 samples.
Sego evaporated cream.	[b]1.033	73.25	26.75	1.45	10.08	8.29	6.95	Sterile; concentrated; no adulterants.
Tulip evaporated cream.	[b]1.034	71.18	28.82	1.57	10.91	9.20	7.14	Do.
St. Charles evaporated cream.	[b]1.076	70.58	29.42	1.88	7.96	11.34	8.21	Do.
Pet evaporated cream.	[b]1.034	72.00	28.00	1.20	9.75	9.91	7.14	Do.
Cows' head evaporated cream.	[b]1.04	67.58	32.42	1.80	10.33	12.19	8.10	No preservatives. Concentrated; sterile.
Ideal evaporated cream.	-------	68.27	-------	1.85	10.10	11.03	7.36	Sterile; concentrated; no adulterants.

[a] Since this table was prepared a number of other milks have been received and their analyses will be found in Table No. 14.

[b] Diluted one-half.

[c] One sample of this cream contained 9.06 per cent of sugar and 20.85 per cent fat.

TABLE No. 12.—*Showing result of examination of samples obtained in the open market of some of the most generally used sweetened, condensed milks.*

Name of condensed milk.	Total solids.	Water.	Ash.	Fat.	Milk sugar.	Proteid.	Cane sugar.	Remarks.
Nestles	25.25	-------	1.84	10.62	12.53	7.90	40.56	Analyzed by Chapin.[a]
Eagle	28.41	-------	1.80	8.44	11.69	7.23	41.52	Do.
Milkmaid[b]	27.43	72.57	1.73	9.63	11.00	4.33	45.88	Milk solids, 26.69.
Perfection	26.86	73.14	1.94	.50	12.06	8.54	50.10	Milk solids, 23.04. A condensed and sweetened skimmed milk.
Meadow brand	23.63	74.37	1.80	4.00	11.55	8.70	48.32	Milk solids, 26.05.
Gold seal	15.23	84.77	1.75	8.25	9.75	7.46	56.57	Milk solids, 27.21.

[a] Chapin: Theory and Practice of Infant Feeding. Second edition.
[b] This milk is popularly known as the "Señorita brand."

The milks which have been tabulated above fall into three principal classes; one of partially concentrated milks, sterilized, bottled, shipped and kept in cold storage, another of pure cows' milk canned without any other alteration than simple sterilization by heat, and the last, of the various types of condensed milks, including the so-called evaporated creams.

1. Cold storage milk.—The only brand of this milk on the market is the "Australian" which, as the name implies, is brought from Australia and the analyses of samples are given in Table No. 11. It is a concentrated milk and the three samples analyzed contained a compound of boron.

2. Sterilized, uncondensed milks are sold in Manila in five brands, and analyses of samples of all are given in Tables Nos. 11 and 15 and the accompanying footnote.[2] These are all free from adulterants and preservatives and, as may be noted from the table, they are without exception excellent, mixed milks. To judge from the homogeneous distribution of the fat and from other considerations it is probable that at least a portion of each of them consists of goat's milk. The proteid constituents of this type have not as yet been carefully examined, but preliminary experiments make it appear probable that the caseïnogen radical is considerably in excess of the normal amount in human milks, as is true in all other milks from the lower animals. However this may be, they are, when properly modified upon a percentage basis, very satisfactory as infant foods, giving as good results as may be obtained with any *sterilized* food. If one of the three brands of pure canned cream on the market

[2] Since this article was finished two new milk products have appeared upon the Manila market, namely, "Natura" and "Butterfly" brands. Analyses of samples of these two brands are as follows:

Name.	Specific gravity.	Water.	Solids.	Ash.	Fat.	Sugar.	Proteid.
Natura milk	1.030	87.00	13.00	0.69	3.22	6.22	2.87
Natura cream	----------	65.57	34.43	.54	27.13	4.34	2.42
Butterfly milk	----------	87.24	12.76	.73	2.92	6.95	2.16
Butterfly cream	----------	64.92	35.08	.62	26.95	4.00	3.51

is used with them, any reasonable percentage formula may be obtained, as will be shown in chapter four, and by the use of such combinations many small patients in Manila who are difficult to feed may be materially benefited.

3. Condensed whole milk.—There is a considerable variety of this class of preserved milks on the market (see Tables Nos. 11 and 15); many are good and some are made from a poor quality of milk, and in a few instances substances have been added which may be deleterious to the health of the consumer. These brands are very extensively advertised and used throughout the Orient for cooking and other household purposes and as a food for infants. They may be so modified for the latter purpose by the percentage method as to make very good substitutes for fresh milk, but when they are simply diluted seven to fourteen times with water, a procedure often recommended and very generally practiced here, they are much too low in fat for the proper nourishment of the infant.[3]

4. Condensed milk, sweetened or otherwise modified.—Analyses some of which are quoted and others made in this laboratory of samples of the principal brands of this class on the Manila market are given in Tables Nos. 12 and 15. Many are honest products, and when they are diluted and modified on a percentage basis, they may be used in the absence of more satisfactory food. These milks all contain large percentages of cane sugar and from some of them a portion of the natural cream has been removed before the process of condensation was begun.

5. Malted milks.—There are two varieties on the market, and copies of analyses of samples of both are given in Table No. 13. These foods are extensively employed in the Philippine Islands and with proper modifications, they can be altered so as to be used as infant foods in many instances. The greatest objection to them lies in the large amount of insoluble carbohydrates which they contain.

6. Cream.—There are three brands of cream sterilized in tins on the market and analyses of samples are given in Table No. 12 and footnote page 373. They are most useful articles in preparing percentage foods from preserved milks, because of the high fat percentage (26+ to 38+ per cent) and the low proteid content in two of them.

[3] Many of the so-called brands of evaporated creams are merely unsweetened condensed milks, having something of the consistency and appearance, but not the taste or physical characteristics of cream. It is asserted by some that concentration to give a sufficient amount of fat warrants the term "cream" as distinct from milk, and that it really makes the product cream, and not condensed milk; but cream does not contain abnormal amounts of casein, lactose and mineral matters, for it is nothing more or less than milk containing an excess of butter fat. The "evaporated creams" contain as many times the normal percentages of all the constituents of milk as there are volumes of milk condensed. It is true that in each case a statement appears on the label that the "cream" is an unsweetened condensed milk, but this information is generally given in such a way as not to attract attention.

(*d*) FOODS OTHER THAN MILK.

We have homemade and imported varieties and diluents of this class.

1. The homemade foods of the Philippine Islands are considerable in number; for the greater part they consist of starch and sugar mixtures. Some of these, which are more or less peculiar to the country, may be mentioned. The rice stick which was referred to above, if it were carefully made and not fed to children too early in life would compare favorably in value with some of the other starch and sugar preparations which sell for high prices.

Coconut milk is used in the Philippines to a limited extent as a food for infants. No literature on the subject is to be found here, but the habit of using it is certainly peculiar to people of the Tropics. The composition of this substance varies much with the age of the coconut from which it comes. Walker [4] notes some of its peculiarities and gives a few analyses, which however were not made with a view of determining its nutritional value as an infant food. This question should be carefully investigated, for coconuts are everywhere present in the Philippine Islands and it is very probable that a valuable enzymic diluent or even food may be found in them. The country contains many fruits which should contain substances much needed in those food mixtures which are sterilized, and which therefore are free from enzymes.

2. Imported foods other than milk are not as yet used to the same extent as they are in many other countries, but there are several varieties on the market, some of these are good in the sense that they are honestly made. Analyses *not made in this Laboratory* of a few which are used in greatest quantity in Manila will be found in the following table:

TABLE No. 13.—*Showing analyses of imported foods other than milk.*

Name.	Analyst.	Moisture.	Fat.	Proteids.	Soluble carbohydrates.	Insoluble carbohydrates.	Ash.
Allenbury's food No. 1	Chapin	5.70	14.00	9.70	66.85	----------	3.75
Allenbury's food No. 2	do	3.90	12.30	9.20	72.10	----------	3.50
Horlicks malted milk	do	2.55	1.41	14.00	63.87	15.68	3.57
Nestles milk food	do	2.18	4.45	10.72	43.84	[a]35.34	1.60
Mellins food	do	4.72	.30	10.10	82.06	----------	3.50
Carmicks soluble food	do	5.69	2.18	16.60	38.21	38.54	2.78
Imperial granum	do	6.04	.72	13.77	3.94	67.46	.49
Ridges food	do	8.12	.48	13.83	5.02	69.24	.53
Health Food Companies barley.	do	10.92	.89	6.98	----------	80.35	.86
Robinson's patent barley	do	9.41	.41	7.46	2.91	78.66	.94
Bordens' malted milk	Holt	3.25	5.41	14.04	74.31		2.99

[a] Starch.

[4] *This Journal* (1906) 1, 58.

3. Diluents are most important aids in infant feeding and they deserve especial notice here, because of the necessity for care as to the quality of water and of the other substances used. The following Table No. 14 gives the contents of a few of the principal diluents used in preparing foods for infants.

TABLE No. 14.—*Giving analyses of a few diluents for baby food (taken from Rotch).*

Substance.	Preparation.	Solids.	Ash.	Fat.	Total Proteid.	Casein.	Lactalbumin.	Sugar.	Starch
Oat meal water	2 oz. cooked ½ hour, finished product 1,000 cc.	3.52	0.03	0.08	0.41	------	------	------	2.99
Do	3 oz. cooked ½ hour, finished product 1,000 cc.	5.21	.05	.11	.47	------	------	------	4.58
Barley meal water.	2 oz. cooked ½ hour, finished product 1,000 cc.	3.48	.03	.02	.54	------	------	------	2.88
Do	3 oz. cooked ½ hour, finished product 1,000 cc.	5.19	.04	.03	.68	------	------	------	4.43
Fat free cows' milk.	----------	------	------	.05	3.55	------	------	5.00	-------
Whey from cows' milk.	----------	------	------	------	------	------	0.90	5.10	-------

The contents of these diluents is not generally considered in percentage feeding, but in feeding infants in the Tropics, where the percentages are not as accurate as they are at home, it appears more advisable to include the contents of such substances as barley water when making the calculations for percentages.

Coconut water as a diluent has already briefly been noticed, and it would seem advisable to study this substance, as well as some others of local use, to ascertain their value and action upon the digestive tract of children.

There is now a voluminous literature on the employment of a solution of sodium citrate as a modifier of the curd in cows' milk used for infant feeding and its great value in this respect has been amply demonstrated. It is not generally employed in the Philippines and we would urge physicians to look more carefully into its merits. Limewater while an excellent modifier of the cows' milk curd in certain cases, is too extensively given and is often employed in too great a concentration.

IV. DIET.

Facts are expressed conservatively in stating that for the last four years an average of 2,500 children under 1 year of age have died annually in the city of Manila for want of sufficient or proper food.

The elucidation of the technical problems in this connection is for members of the medical and chemical professions. A study of the available supply of infant food in Manila is necessary and in the preceding pages an effort in this direction has been made, but the weapons provided by this discussion are to be used by all the people. A successful administration looking to the improvement of conditions can only be furnished by extensive organization and education. Members of our profession in Manila are often indifferent in questions of infant feeding. This is shown by the fact that there are but *very* few records of examinations of milks, either human or animal, to determine their nourishing properties, to be found in the laboratories of the city.

There is, therefore, entirely too much left to chance in the composition of the foods recommended and not enough adjustment of food values to special conditions as they are represented by individual patients. Directions should be very specific and given in writing. It is not enough to order a mixture of condensed milk and limewater to be given from a boiled bottle. The average, or even the most ignorant, mother knows how to prepare such mixtures herself, as she can read the directions on the label of the can of milk. We must far more closely study each infant and order a food which will properly nourish the child or remove the abnormal condition.

The service of one of us at St. Paul's Hospital has shown some of the most serious of errors in very general use, one which we wish especially to call attention to, namely the use of excessive quantities of limewater as a diluent. This is a very common practice, and many of the patients suffering from proteid starvation and chronic diarrhœa, marasmus, gastric atony, etc., are more apt to have the trouble caused by an exces of lime than by any inherent difficulties in the milk administered.

The preparation of infant foods for all kinds of the many conditions encountered is a difficult task, which can best be undertaken by milk laboratories similar to those now in use in many American and European cities. This procedure would cost a considerable amount of money, but with organization and education, funds might become available either through the Government or by gifts from philanthropic sources.

A discussion of the conditions confronting us in Manila together with analyses of food stuffs has been given in chapter three, and in order to give a more clear understanding, the following Table No. 15, representing a majority of the varieties of food supply obtainable in Manila, is inserted.

TABLE NO. 15.—*Showing the essential facts taken from analyses of samples of milks and other most generally used infant foods available in Manila together with some normal working standards.*

Substance.	Fat.	Milk sugar.	Total proteid.	Casein.	Lact albumin.	Soluble carbohydrates.	Insoluble carbohydrates.
Average human milk (Rotch) [a]	3.00–4.00	6.00–7.00	1.00–2.00	0.59	1.23		
Average human milk (König) [a]	3.80	6.20	2.30	1.00	1.30		
Average milk, Caucasian woman, Manila.	4.24	6.63	1.45				
Average milk, Filipino woman—							
Of better class, Manila	5.38	6.83	1.45				
Of lower class, Manila	3.07	7.98	1.29				
Average cows' milk (Rotch) [a]	4.00	4.75	3.50	2.66	.84		
Average cows' milk (König) [a]	3.70	4.90	3.50	3.00	.50		
Average cows' milk, Manila	2.82	4.21	3 15	4.70			
Average goats' milk (Rotch) [a]	4.30	4.00	4.70				
Average goats' milk (König) [a]	4.80	4.40	4.30	3.20	1.10		
Average goats' milk:							
Native, Manila	5.73	3.54	4.05				
Maltese, Manila	4.75	4.27	3.23				
Average carabao's milk	10.65	3.73	6.31				
"Bear milk"	4.27	4.06	3.07				
"Dragon milk"	4.12	4.35	3.11				
"Weribest milk"	3.24	4.75	3.10				
"Bear cream"	38.07	3.27	2.29				
"St. Charles evaporated cream"	7.96	11.34	8.21				
"Highland evaporated cream"	7.86	11.13	8.40				
"Sego evaporated cream"	10.08	8.29	6.95				
"Tulip evaporated cream"	10.91	9.20	7.14				
"Bear concentrated milk"	9.67	9.79	7.84				
Australian (cold storage)	14	13.52	9.31				
"Pet evaporated cream"	9.75	9.91	7.14				
"Cow's head evaporated cream"	10.33	12.19	8.10				
"Ideal evaporated cream"	10.10	11.03	7.36				
"Nestles condensed milk"	10.62	12.53	7.90			[b] 40.56	
"Eagle condensed milk" [a]	8.44	11.69	7.23			[b] 41.52	
"Milkmaid condensed milk"	9.63	11	4.33			[b] 45.88	
"Gold seal condensed milk"	8.25	9.75	7.46			[b] 57.56	
"Perfection condensed milk"	.50	12.06	8.54			[b] 50.10	
"Meodora condensed milk"	4	11.55	8.70			[b] 48.32	
"Allenbury's food No. 1" [a]	14		9.70			[b] 66.85	
"Allenbury's food No. 2" [a]	12.30		9.20			[b] 72.10	
"Nestles milk food" [a]	4.45		10.72			[b] 43.84	[c] 35.34
"Mellins food" [a]	.30		10.10			[b] 82.06	
"Carmicks soluble food" [a]	2.18		16.60			[b] 38.21	[c] 38.54
"Imperial granum" [a]	.72		13.77			[b] 3.94	[c] 67.46
"Ridge's food" [a]	.48		13.83			[b] 5.02	[c] 69.24
"Health Food Companies barley" [a]	.89		6.98				[c] 80.35
"Robinson's patent barley" [a]	.41		7.46			[b] 2.91	[c] 78.66
"Borden's malted milk" [a]	5.41		14.04		74.31		
"Horlick's malted milk" [a]	1.41		14		63.87	[b] 15.68	
Oat meal water (Rotch) [a]	.08		.41				[c] 2.99
Do. [a]	.11		.47				[c] 4.58
Barley meal water (Rotch) [a]	.02		.54				[c] 2.88
Do	.04		.68				[c] 4.43
Fat free cows' milk (Rotch) [a]	.05	5	3.55				
Whey from cows' milk (Rotch) [a]		5.10			.90		

[a] Analysis not made in this laboratory. [b] Cane sugar. [c] Starch.

It has been shown that fresh milk is practically at present eliminated from our armamentarium, and with this fact before us text-books on infant feeding become almost valueless just at the point where our problem begins. This condition is of course largely responsible for the confusion, each man being to a great extent thrown upon his own resources.

The most generally used foods among the better classes have mainly been the so-called evaporated creams, diluted four to ten times with water, with perhaps the addition of an indefinite amount of limewater and sugar. When diluted sufficiently to give a suitable proteid percentage, the fat and sugar are far below the requisite amount. While the addition of milk sugar or cane sugar makes up one of the deficiencies, the fat percentage remains low, and as a result constipation and other defects of nutrition are very frequently observed. In many instances various mixtures of milks and of foods containing starch and sugar are concocted; these overcome the constipation, but they still leave the fat deficient, or the proteids too high and thus other and more serious disturbances arise.

Inasmuch as conditions are such as to make the employment of preserved milks imperative in the feeding of infants, it is necessary to use these substances to the best advantage. To accomplish this end our experience has shown us that it is better to disregard the claims and directions of the milk manufacturers, to analyze their products carefully and by careful combinations to *institute percentage feeding with the use of these artificial foods.* It is remarkable what may be done in this way with patients presenting the greatest difficulties in feeding.

However, in order to secure the best results with this percentage feeding of artificially prepared milks a most important prerequisite is constantly to impress upon mothers and nurses the necessity of the supervision of the physician. It is justifiable to explain to the mother that feeding of the infant is a more strictly medical matter than is even medical supervision at the birth of the child. Absolutely nothing should be fed except what is prescribed *in writing* by the physician and if members of the family are taught this from the birth of the infant and their confidence is assured by a carefully prepared formula for feeding, but little difficulty will be experienced in controlling the situation and insuring the health of many babies who would otherwise perish from dietetic errors. For this percentage feeding in Manila our armamentarium consists principally of the following substances:

1. Plain, sterilized, uncondensed milks: There are five brands on the market.

2. Pure creams: There are three brands on the market.

3. Sugars: Lactose and saccharose.

4. Diluents: The usual varieties of barley water, oat-meal water, lime-water and sodium citrate solutions.

5. Peptonized milks, butter milks, fat free milk and the other usual modifications of fresh milk may nearly all be made in a fairly satisfactory manner from the fresh, sterilized milks mentioned above by the use of appropriate ferments and other methods.

6. In place of the plain sterilized milks, condensed whole milks or the so-called evaporated creams which are in reality only condensed whole milks, may be used provided the percentage method of dilution is used and the deficient fat made up by the addition of cream.

7. In special cases and where price is an object, the condensed sweetened milks may be used by following the percentage methods in dilutions and by the addition of cream to replace the deficient fat.

All the milks which have been mentioned have been carefully analyzed either in this laboratory or by other authorities and the averages shown in Tables Nos. 11 and 15 may be used as sufficiently accurate for practical purposes.

By using these averages and figuring on 100 cubic centimeters of finished product as a percentage basis, calculations are easily made and the only vessel necessary in preparing the food is a clean, graduated, glass cylinder; one of 1,000 cubic centimeters capacity will be found most useful.

The rich, tinned creams do not keep very well after the can is open and for that reason it is well to prepare an entire day's feeding at one time, fill it into the necessary number of clean nursing bottles, plug with cotton and keep in the ice box until ready for use.

Some prescriptions for percentage feeding are given below, but in order to make the subject still more clear the following example is submitted.

Suppose it is desired to give an infant 1½ months old, eight feedings of 100 cubic centimeters each in twenty-four hours, each feeding to contain fat 4 per cent, sugar 7 per cent and proteid 1 per cent. By simple calculation or by reference to the Cox chart number 1 we find that 1 per cent proteid and 4 per cent fat may be obtained by using 24 cubic centimeters of one of the above-mentioned sterilized milks and 11 cubic centimeters of one of the 27 per cent creams or 7½ cubic centimeters of the 38 per cent cream to each 100 cubic centimeters of finished product, or 192 cubic centimeters of milk and 88 or 60 cubic centimeters of cream for the entire day's feeding of 800 cubic centimeters. Simple calculation shows that this substance will contain but 1.6 per cent of sugar and this deficiency may be made up by the addition of 5.4 grams of milk sugar per 100 cubic centimeters of finished product.

Having determined the necessary amounts of the different substances to be used in the finished product, a prescription should be written showing these amounts and the percentages of each ingredient. The mixture is best made in the following manner:

Place the necessary amount of distilled or boiled water in the graduate, add the milk sugar and stir with a clean glass rod until solution is complete, next add the requisite amounts of milk and cream and stir again. Finally, add the limewater, sodium citrate or other modifier, stir and pour the product directly into the necessary number of clean nursing bottles, stopper with clean cotton and place in the ice chest until ready for use.

When using sodium citrate in the food it is best to prescribe a 3 or 5 per cent solution to which a few drops of chloroform have been added to prevent bacterial decomposition.

With little care, any reasonable percentage food may be made according to the above method and we need not at this day emphasize the confidence with which such known percentages are fed, nor the excellent control which a knowledge of *just* what the infant is being fed gives us over many of the more frequent disturbances which food often causes in infants.

Both the manner of percentage feeding, and its results may be further shown by a few illustrative cases.

CASE 1.—*Four months old, weight 9⅛ pounds, anæmic, wasted, diarrhœa with excoriations about anus, mucous membranes of mouth red and inflamed, abdomen prominent, vomiting of food, fretful and crying much of the time. Percentage feeding instituted with rapid gain in weight and complete recovery.*

This baby was a normal child at birth, weighing 8 pounds. The mother's milk was reported to be deficient in quantity from the beginning but no examinations were made. At 2 weeks of age alternate feedings of breast milk and a certain condensed milk were instituted, the milk being prepared according to the directions of the manufacturer. No improvement followed and at 5 weeks of age another milk was tried. Still the baby failed to improve and during the next ten weeks the giving of still another brand of artificial food was instituted. When the baby came under our observation a dose of castor oil was given and all food withheld for twenty hours, after which a prescription was given of sterilized milk, pure 27 per cent cream, milk sugar and sodium citrate in such proportions as to give a little less than the normal percentage of fat, sugar and proteid. The child enjoyed the food, did not vomit and improvement was rapid from the date the feeding was instituted. By altering the amounts of "milk" and "cream" which were used, the percentages of the fat, sugar and proteid were changed so that at 5½ months of age the child was taking normal amounts and was in excellent health; he passed from observation at 8 months of age. A study of the mother's statements about the amount and kind of food previously given in connection with the analysis given in Table No. 15 shows that this baby had been receiving too much proteid (3½ per cent) and sugar (8 per cent) and not enough fat (1.8 per cent), and in addition 10 per cent limewater was being used.

CASE 2.—*Four months of age, weight 12 pounds, fretful and crying, fontanelles sunken, muscles wasted, constipation, head perspiring, tender joints and back,*

takes food irregularly, followed occasionally by vomiting. Percentage feeding instituted with rapid recovery.

Because of failure of breast milk this normal 8½-pound baby was given substitute feeding at 3 weeks of age consisting of an "evaporated cream," prepared according to the directions of the manufacturer. There was no improvement and when the infant came under observation it was receiving a one-fourth dilution of this milk plus 10 per cent limewater and 5 per cent milk sugar. Figuring from our Table No. 15 we see that this baby was taking about as follows: fat 2.5 per cent, sugar 9 per cent, and proteid 2.75 per cent. The proper percentages were instituted here by simply combining a 38 per cent preserved cream with a *proper amount* of the same excellent food the baby had been receiving, with the addition of the necessary sugar and the changing of the limewater to a solution or sodium citrate.

The trouble with this patient as with the other and many more whom we could enumerate, was the lack of proper proportions of the essentials in the food, and this lack was largely due to the want of appreciation of what was necessary and to a manufacturer's claims for the superiority of his milk.

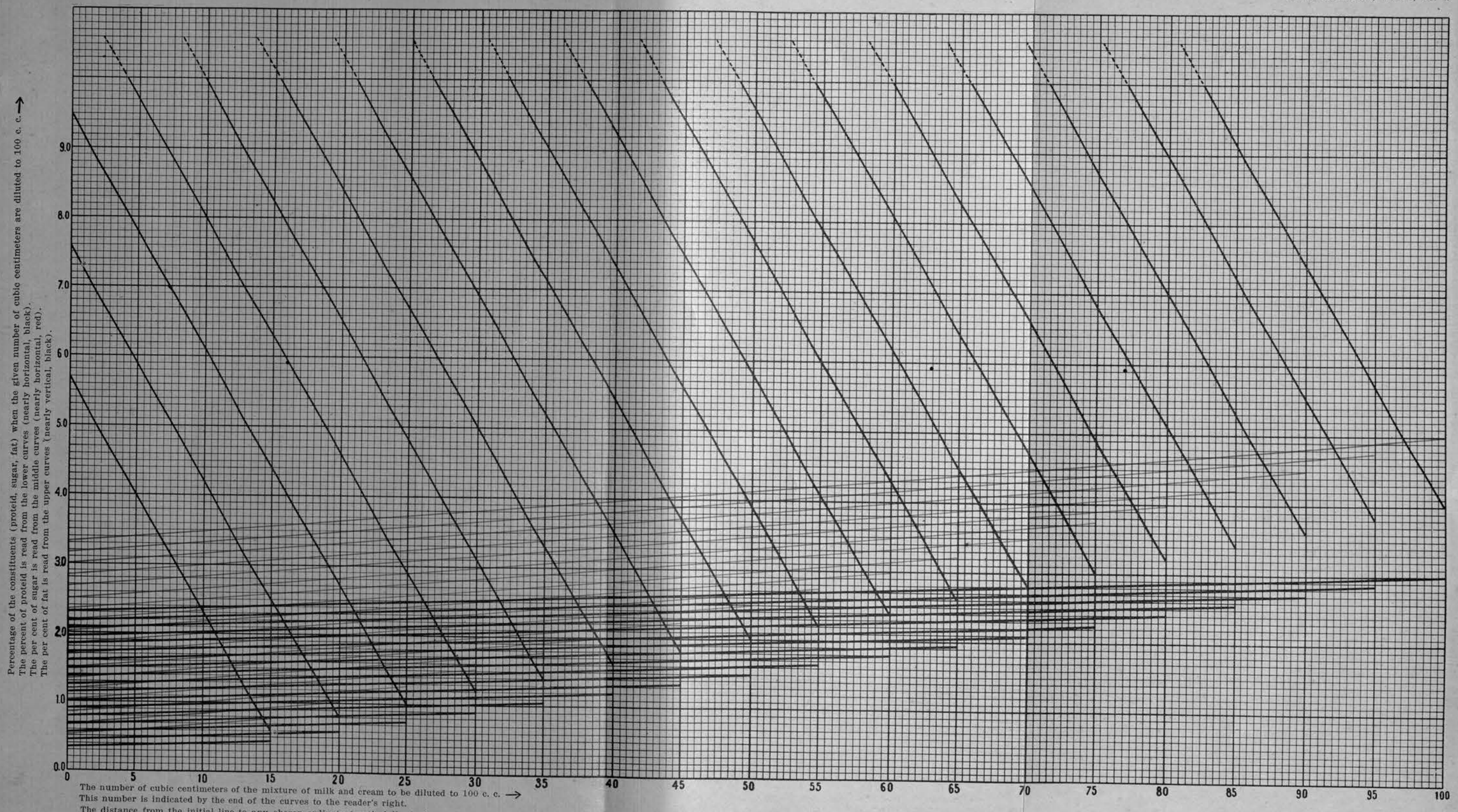
By proper adjustments of amounts of the various brands of sterilized, pure cow's milk, evaporated or condensed milks and preserved and condensed creams, a fairly wide variation of percentages may be made and it is in this way that we may obtain the best results from feeding preserved milks. What is most needed on the part of manufacturers is the giving of more accurate information concerning the composition of their foods and their methods of preparation, with fewer statements about what they will accomplish. Special results in special cases are more the result of elasticity in the babies' metabolism than in any unique composition which may be given to any one brand of cow's milk evaporated *in vacuo*.

Chart No. 1, opposite this page, which has been prepared for us by Dr. A. J. Cox, Chemical Laboratory, Bureau of Science, taken in conjunction with Table No. 15, will help the physician in calculating his percentages from the principal milks to be found in the Manila market:

Explanation of Chart No. 1.[5]—The fact that children of different ages require milks of different composition for their proper nourishment, makes it very desirable that we have some way of quickly ascertaining the proper mixture of milk and cream and its dilution. The old cut and dried method is unsatisfactory and extremely slow because of the great number of variable factors involved.

The very close agreement between the analyses of all the brands of pure, sterilized milks for sale on the Manila market makes it possible to prepare a chart from which the amounts of lactose, water, milk, and cream which will give the proper percentage of constituents in the final product, may be calculated when any one of these milks and any standard pure cream are used. The chart is prepared on the basis of a 38 per cent cream, but as is explained blow it is equally well adapted for the

[5] By Dr. A. J. Cox.



The distance from the initial line to any chosen ordinate (vertical line) shows the number of cubic centimeters of milk and from this ordinate to the end of the curves shows the number of cubic centimeters of cream. These numbers are chosen so as to give the composition desired. These compositions—that is, the percentages of proteid, sugar, and fat—are shown by the points where the chosen ordinate representing the relations between milk and cream cuts or intersects the proteid, sugar, and fat curves, respectively, which have their lower termini in the ordinate representing the number of cubic centimeters of the mixture to be diluted to 100 c. c.

CHART No. 1.

27 per cent creams which are now on the market. The average of the pure sterilized milks[6] previously mentioned has been taken as—

	Per cent.
Fat	4
Sugar	5
Proteid	3

The average[7] of the analyses of several samples of the 38 per cent cream is as follows:

	Per cent.
Fat	38
Sugar	3.3
Proteid	2.3

It will be seen that the percentage of proteid is roughly the same in both milk and cream, so that for young children the desired low proteid content may be obtained simply by dilution of either of these, but this would not suffice for the content of fat. If milk alone were diluted the fat would be too greatly reduced and if the cream alone were used it would be too high, but by using both milk and cream a mixture may be obtained which will also give the desired fat content.

Enough sugar of milk may then be added to increase this constituent to the percentage desired: or better still, after the factors are established, dissolve the sugar of milk in the water before adding the milk and cream, for then one can see that a perfect solution is attained.

For the mixture of cream with milk the percentage of each constituent varies from that of the milk toward that of the cream directly in proportion to the amount of cream added, that is, a straight line joining the percentages of a constituent in the milk and the cream gives all the possible variations for the percentage of that constituent. Now, if this mixture is diluted with water we would get the same result divided by the amount of dilution, or a curve (straight line) parallel to the former with its lower end terminating on the number of cubic centimeters of the mixture which was diluted to 100 cubic centimeters. These results have all been expressed in the chart. In the chart, the curves have been made for variations of 5 cubic centimeters in the total mixture of milk and cream to be diluted to 100 cubic centimeters. Closer results could be obtained if 1 cubic centimeter variations had been plotted, but the network of

[6] If one of the sterilized pure milks is not at hand, a milk of approximately the same composition may be had by diluting a volume of any of the better class of concentrated milks, or "evaporated creams" shown in Tables No. 11 and 15, with 1½ volumes of distilled water, that is, every 40 cubic centimeters should be diluted to 100 cubic centimeters and this may be used instead. Any good quality of (Maltese) goat's milk may also be used.

[7] One sample which contained 20.8 per cent fat and 9 per cent sugar was not included in this average.

curves would have been confusing. The curves as they are given only approximate the desired results, but they are accurate enough for all practical purposes.

These being the data, the following example is explanatory: For an average child six weeks old we desire a milk of the following composition:[8]

	Per cent.
Fat	4
Sugar	7
Proteid	1

We may start with either the desired proteid or fat content. Let us take the proteid simply because these curves lie closer together and it is easier to differentiate at the beginning. For 1 per cent content we have two possibilities, either the curve which terminates in the 40 or the one in the 35 cubic centimeters of total mixture of milk and cream to be diluted to 100 cubic centimeters. Let us first consider the former. If we follow the fat curve for this mixture to 4 per cent, the ordinate at that point does not cross the proteid curve at the desired point, namely, 1 per cent. If on other hand we take the fat curve for the 35 cubic centimeter mixture and follow it to 4 per cent, we find the ordinate to cut the proteid curve at 1 per cent content, and this shows us the proper relation to be 27½ cubic centimeters of milk and 7½ cubic centimeters of cream. Now the sugar of milk curve which terminates on 35 cubic centimeters intersects the chosen ordinate 27½ at 1.6 per cent. This gives us the sugar content of the mixture of milk, cream and water. We desire 7 per cent. It is necessary then to add as many grams of sugar of milk as the difference between the desired and actual sugar content, namely, 7 minus 1.6 or 5.4 grams per 100 cubic centimeters. Therefore the desired amounts of each are as follows:

Water	cubic centimeters	65
Milk	do	27½
Cream	do	7½
Sugar of milk	grams	5.4

If a pure cream with a fat content other than that which is the basis of the chart,[9] namely 38 per cent, is used, then a correction in the quantities of milk and of cream as given above is necessary. If a cream with

[8] Rotch, T. M.: Pediatrics (1906), 196.

[9] Two such samples have recently appeared on the Manila market namely "Natura" and "Butterfly Brand." The analyses of single samples of these made by this Bureau are as follows:

	Natura.	Butterfly.
Fat	27.1	26.95
Sugar	2.3	4.00
Proteid	2.4	3.51

a fat content lower than 38 per cent is used, then in order to give the desired composition the cubic centimeters of cream must be *increased* to

$$\frac{38-4}{(\text{The per cent of fat in the cream used})-4} \times \text{The number of cubic centimeters of cream given by the chart.}$$

and the cubic centimeters of milk *diminished* by the amount of the increase in the quantity of the cream. If a cream with a fat content higher than 38 per cent is used, then the cubic centimeters of cream must be *diminished* to

$$\frac{38-4}{(\text{The per cent of fat in the cream used})-4} \times \text{The number of cubic centimeters of cream given by the chart.}$$

and the cubic centimeters of milk *increased* by the amount of the decrease in the quantity of the cream. The proteid and sugar of all pure creams have approximately constant values, so that for these the chart is always applicable and no appreciable error is produced when the correction for fat is made.

Let us consider what the results of the above example would be were a 27 per cent cream to be used instead one of 38 per cent. The percentage of fat in the former is lower than it is in the latter, therefore the cream required would be increased to $\frac{38-4}{27-4} \times 7.5$ or 11 cubic centimeters, an increase of 3.5 cubic centimeters over the quantity of 38 per cent cream. The milk would be diminished by 3.5 cubic centimeters or reduced to $27.5-3.5$ or 24 cubic centimeters. Hence, the desired amounts of each ingredient to give a milk of the above composition when a 27 per cent is used would be—

Water	cubic centimeters	65
Milk	do	24
Cream	do	11
Sugar of milk	grams	5.4

If it is desired to add lime water (sodium citrate, etc.) then the water content should be diminished by the number of cubic centimeters of lime water (sodium citrate, etc.) to be added. If more than 100 cubic centimeters of the mixture is desired, multiply the quantities of water, milk, cream, and sugar of milk respectively by as many times as the quantity desired is greater than 100.

GANGOSA IN THE PHILIPPINE ISLANDS.

By W. E. MUSGRAVE and HARRY T. MARSHALL.

OUTLINE.

I. Clinical report.
II. Autopsy report.
III. Résumé of literature.

Gangosa has not previously been reported for the Philippine Islands. Because of the comparative rarity of the disease, its limited geographical distribution and probably infectious nature, the following case is of sufficient importance to warrant discussion. The patient was seen several times by Dr. N. T. McLean, United States Navy, who has had a large experience with the disease in Guam, and the diagnosis was confirmed by him.

I. CLINICAL REPORT.

Case record.—Gangosa; death; autopsy.—The patient, C. F. (2179) was admitted October 31, 1906, to Dr. McDill's service in St. Paul's Hospital. He was transferred to Dr. Musgrave's service on December 15, 1906, and died January 23, 1907. He was a Filipino, male, 29 years old, single and a native of Santo Domingo de Basco, Batan Islands.[1] The patient was an unusually ignorant native of the lower classes and the value of his statements was not very great. However, the following facts obtained at different times and repeated to different interpreters are probably true. Father, mother, and two brothers are living and in good health. The patient stated that none of his relatives has a disease like his but he was equally positive that several other people in the same town are suffering from a similar condition. Previous diseases were denied. The patient stated that he was never far from his native town until he came to Manila two years ago and that he had never been ill except once with *calentura* (fever). The last two years before entering the hospital he resided in one of the barrios of Manila and worked as a stable boy most of the time.

[1] The *Batanes* constitute the most northern group of the Philippine Islands. They lie about 120 miles due north of Luzon.

His statements about the time of the onset of his present illness differed very much, but Dr. Ariston Bautista y Lim, who saw him, thinks it was probably about five years ago that he first noticed sore throat and that the disease had been gradually growing worse since that time. He had taken many kinds of medicine during the last two years without any improvement. On admission to the hospital the patient was considerably emaciated and anæmic, the voice had the intonation peculiar to destructive conditions of the larynx and soft palate and there was an opening about 1 centimeter in diameter in the bridge of the nose. Upon closer examination it was found that the uvula was partially destroyed and the palate had two dirty, grayish-appearing, perforating ulcers. The pharynx, upper larynx, palate, posterior nasal structures, both bone and soft tissues, were partially destroyed by a chronic type of ulceration and there was a considerable amount of scar tissue, showing some evidences of repair. The margin of the upper lip was also destroyed, leaving a grayish, granular surface. The odor from these lesions was exceedingly offensive and there was at times a slight discharge of granular, necrotic material. Microscopic examination of fresh and stained smears, made by scraping the surfaces of the wounds, were negative for acid-fast bacilli and for treponema. During the period of observation the nasal wound increased in size, there was more deformity due to destruction of bone, and the destructive lesion on the upper lip progressed slowly until death. Plate 1 is from a photograph made about one month before the fatal termination. There was diminished sensation over the surfaces of the wound, which in places amounted to local anæsthesia.

The skin was otherwise rough but apparently free from disease or scars. About five weeks before death a dull, chronic-appearing skin ulcer developed on the outer side of the left shin and this continued slowly to extend until death, at which time it was about 1 centimeter in diameter and extended through the skin. The superficial lymphatics were slightly enlarged in the groins, but not more so than is commonly seen among the lower classes of barefoot people here. The muscles were wasted, the joints were free from disturbance and except as above noted, no bone lesions could be found. No abnormalities were found in the circulatory system except an anæmic murmur of the heart. Temperature was normal and there was but slight fever at any time during which the patient was under observation, which was nearly three months. Two days after admission there developed an irregular, intermittent fever varying between normal and 38°.5, which lasted for a few days, and again, just preceding the fatal termination, there was slight pyrexia. A blood examination on admission showed no leucocytosis and no abnormal elements. A blood examination five days before death showed no malaria; leucocytes 11,600, hæmoglobin 80 per cent.

Differential count.

	Per cent.
Small lymphocytes	10.0
Large lymphocytes	4.6
Polymorphonuclears	82.0
Eosinophiles	2.6
Basophiles	.4

There was slight cough at times during the patient's stay in the hospital, but it was never annoying and the expectoration, if any, was swallowed. A physical examination of the chest on admission showed signs of some bronchitis. There were no subsequent examinations. The sputum was not examined because none could be obtained. The tongue was constantly coated with a heavy, brownish fur, but no ulceration took place. The appetite was poor, the patient had to be fed largely by a tube, there was no vomiting or pain. The bowels were constipated, moving but seldom except from cathartics or enemas. Microscopic examination of the feces showed ova of *Trichuris trichiura.* There were no disturbances of the urinary function. Examination of the urine showed a trace of albumin and a few hyaline casts. This patient never complained of pain; as a rule sleep was sufficient, but during the last week of his illness there was considerable restlessness and insomnia. The reflexes were normal. The eyes were apparently normal, but hearing became somewhat defective toward the end. The sense of smell was almost *nil* and speech was of the Gangosa type, its peculiarity resulting from destruction of the palate.

Treatment.—A probable diagnosis of syphilis was made when the patient was first admitted to the hospital; antisyphilitic treatment was instituted and continued for three months. This treatment consisted of intramuscular injections of mercury to the point of toleration, of potassium iodide by mouth and intravenously in doses up to 10 grams per day. Mercury was also tried by inunction.

The antisyphilitic treatment did not cause any improvement and it was discontinued after three months. This was followed by copper sulphate in 0.015 doses, three times a day for about one month without any improvement and no further specific therapeutic measures were undertaken. Death occurred January 23, 1907. *Clinical diagnosis, Gangosa.*

II. AUTOPSY REPORT.

Autopsy.—Four hours after death. The body is markedly emaciated, rigor mortis of moderate grade present, one old, grayish colored ulcer on the left leg about 8 millimeters in diameter extends to the deeper layers of the skin. The muscles are wasted and pale. The *superficial lymphatics* in the groins moderately enlarged, pale in color and quite firm.

The *left lung* contains a few, reddish-colored infarcts from 7 millimeters to 1 centimeter in diameter, mostly in the lower lobe. There is

an old, adhesive pleuritis on the right side; the *right lung* contains several areas similar to those in the left and there is also a small tuberculous cavity in its apex. There is a moderate bronchitis, and a few areas of beginning broncho-pneumonia in both organs. Nothing abnormal is found in the *heart* or its membranes.

The *abdomen* is free from adhesions, the tissues and organs appear to be anæmic and with slight enlargement of some of the mesenteric lymphatics. No marked departure from the normal is seen in any of the organs except the *stomach*. This shows a general hemorrhagic catarrh of the mucosa.

In order to preserve good museum specimens, the soft tissues of the neck were divided at the upper end of the sternum, carefully dissected up from the cervical column and the latter cut by sawing through the first cervical section. The brain was removed, but nothing abnormal was found in this organ. The rest of the head and soft tissues of the neck were placed in formalin for two days and then, after hardening, they were divided antero-posteriorly in the median line. By this method a careful study of the lesions of both bone and soft tissues was made possible.

In these specimens a condition typical of that described for gangosa is found. There is marked destruction and some scar formation of the soft parts, including the larynx, pharynx, soft palate, uvula and nasal tissues. The nasal septum and a considerable area in the bridge of the nose, including both bone and cartilage, are destroyed. The palate is also partially destroyed. The process in addition has extended into the sinuses of the cheek bones and here it has included both bone and soft tissues. There is no evidence of acute inflammation, the surface of the destroyed areas is covered with a dirty, granular material, which when removed leaves a gray, sponge-like tissue. Scrapings from the diseased areas are free from acid-fast bacilli and treponema.

Smears from the pneumonic areas in the lungs showed a single filarial embryo but no others were observed during the examination of many preparations from similar locations.

Anatomic diagnosis.—Chronic ulceration of the naso-pharyngeal tissues including destruction of the palate, nasal septum, turbinates and involvement of the maxillary sinuses; together with extensive destruction and scar formation of the adjacent soft parts of the larynx, pharynx and nasal tissues. Tuberculosis of the right lung with a small cavity in the right apex. Terminal broncho-pneumonia. Moderate lymphadenitis, more marked in the region of the neck. Acute hæmorrhagic catarrh of gastric mucosa.[2]

[2] The only other autopsy which has been made upon a patient with gangosa is one reported by Mink and McLean. In their case, a male of 18, the entire nasal passages, hard and soft palate were destroyed; the tonsils and pillars were replaced by scar tissue; there was cardiac hypertrophy, and fine adhesions existed between the lungs and pleuræ. The diagnosis in their case was "native epidemic asthma."

HISTOLOGY.

Ulcer I, edge of skin, hæmatoxylin and eosin.—On surface of ulcer there is a structureless, necrotic membrane, cloudy and purplish, in which one can dimly make out degenerated cells. Necrotic processes extend from this membrane into clefts in the tissue beneath. The transition is sharp between the necrotic membrane and the subjacent, richly cellular tissue. The latter is a loose, vascular, arcolar tissue containing a moderate amount of fat and supported by heavy trabeculæ of connective tissue. A few strands of degenerating voluntary muscle are found in the deeper part of the section. The loose fatty tissue is black from accumulations of small round cells, which are abundant just at the necrotic border and diminish in numbers as the distance from the edge of the ulcer increases. Mingled with the small round cells are a few large mononuclears, larger epithelioid fibroblasts, and numerous plasma cells with small, eccentric, dark nucleus and fairly abundant irregular bluish protoplasm.

The necrotic process is evidently advancing and has already involved several vessels. One of these, a small artery, is plugged with a hyaline mass and its walls can no longer be made out because of the dense, small, round cell infiltration, but near by a wide, thin-walled sinus shows no obliteration at all. With the exception of the small artery above mentioned, and one other artery near the advancing edge of the ulcer, in which the same process is occurring, there is no special accumulation of round cells around the vessels.

The muscle in the deeper part of the section is undergoing necrosis, and in large measure has become converted into a homogeneous or finely granular, bright-red mass, with fine nuclear fragments scattered through it.

At the edge of the ulcer there are two irregular downgrowths of stratified epithelium, one nearly a millimeter in length. In each of these areas the upper layers are of irregular thickness and composed of large, poorly staining cells, often vacuolated, in which the nuclei show various irregularities. The deepest layer of cells is as a rule uniform in arrangement and staining, the downgrowths being no more atypical than those in a benign papilloma of the skin. However, along one side there are several delicate, finger-like projections of epithelium entering directly into the underlying tissue, the protoplasm extending beyond the last nucleus to form a protoplasmic mesh work in which several small, round cells are gathered. The arrangement makes it difficult to determine exactly where the epithelium ends and connective tissue and infiltrating cells begin.

One of these epithelial areas is definitely retracted from the adjacent tissue, and this shows no downgrowths.

There are none of the irregular nuclear figures nor epithelial pearls which occur in epithelioma and the nuclei of the cells of the deepest

layer of epithelium remain fairly characteristic, in spite of the irregular protoplasmic downgrowth. It is to be noted that the nuclei of the epithelial cells do not invade the underlying tissue, the downgrowth being altogether protoplasmic.

Sections B, C, D, E, F, and G, taken from different parts of the ulcerating area between the anterior nares and the pharynx, have much the same appearance, and are characterized by advancing necrosis with very little reaction on the part of the tissue. The necrosis is advancing upon areolar tissue, upon mucous glands, voluntary muscle, etc. In only one case is there any decided reaction, and that is found in a section taken evidently at the junction of the ulcer and face. The section passes through the edge of ulcer and adjacent skin. At a distance from the ulcer the epithelium is delicate and thin, pigment is abundant, the deepest layer of cells is uniform, the under surface of the epithelium is fairly even, with only a few small papillæ. The hair follicles, sweat glands, sebaceous glands and subcutaneous tissue appear normal. As the edge of the ulcer is approached, the subcutaneous tissue becomes slightly œdematous and finally infiltrated with cells. The epithelium becomes thicker and thicker, the horny layer reduced, the epithelial pegs longer, thicker and more irregular, and the pigment disappears. Just at the edge of ulcer the epithelium dips down as an irregular peg, 1 millimeter into the subcutaneous tissue. The epithelial cells are large, cloudy and pink, often vacuolated, the nuclei are vesicular, pale, uniform and do not show the irregularities met with in epithelioma.

Over the ulcer there is a thin layer of necrotic, granular, pinkish material, beneath which lies a narrow zone of disintegrating cells, red blood corpuscles, etc., immediately followed by a richly cellular and vascular granulation tissue. In this tissue there are many capillaries, round and elongated fibroblasts, disintegrating red blood corpuscles and much yellow blood pigment, and a fairly large amount of fibrillated intercellular material. In the outer border of the granulation tissue there are a small number of lymphocytes and cells with small, round, dark nuclei and fairly abundant pink to purple protoplasm, the nucleus being sometimes central, sometimes eccentric. Extravasated red corpuscles and yellow blood-pigment are found as far as the deepest limits of infiltration. There is no evidence of perivascular infiltration. There are no polymorphonuclear leucocytes, excepting at the necrotic edge of ulcer.

The granulation tissue is less than 2 millimeters at its thickest part. There is an abrupt transition from this to the slightly œdematous, fatty subcutaneous tissue. Within 2 to 3 millimeters of the surface of the ulcer two large arteries are found with their walls very œdematous, and the lumina becoming obliterated. At some distance below the end of infiltration there is found a strand of young granulation tissue and plasma cells, but there is no evidence of the occurrence of young foci

of necrosis beyond the advancing edge of the ulcer. This section differs from the others in the relative abundance of granulation tissue. In the other sections there is very little granulation tissue formed.

In sections stained by the Weigert-Gram method and for tubercle bacilli there is nothing characteristic. No acid-fast bacilli are found. There are a number of cocci, mostly diplococci, and a few slender, blue-staining curved rods on the free surface of the ulcer; elsewhere no bacteria.

The heart.—Stains well; the structure is well preserved; the epicardium slightly œdematous; in the meshes are scattered a few small, round cells and occasionally, cells with red protoplasm; the muscle fibers also are quite widely separated, the intervening spaces being clear or containing small amounts of pale, pink, granular or fibrillated material but no leucocytes. The vessels are normal and show no perivascular leucocytosis.

The protoplasm takes a bright eosin tint; striation and fibrillation are distinct; the muscle nucleus is surrounded by an oval, clear space two to five times the length of the nucleus, containing only a slight amount of brownish pigment. This central clear space often makes the fibers which are cut on longitudinal section appear to be split, and in general the muscle fibers are drawn out into longer and narrower ribbons than usual. The nuclei are small, fairly uniform, pale and vesicular with a darker nuclear capsule and a variable number of chromatin dots. A moderate number of fibers show myocardial fragmentation with the stair-like arrangement of fibrils.

Lung, hæmatoxylin and eosin and tubercle stain.—Typical, acute broncho-pneumonia is shown in one section. Some alveoli are nearly clear; others contain coagulated albumin. Congestion, œdema and desquamation also occur; in other places there are consolidated areas in which the alveoli are packed with polymorphonuclear leucocytes, red blood cells and fibrin in varying amounts, fibrin being unusually abundant. A bronchiole cut in the section has its wall infiltrated with polymorphonuclears and its lumen stuffed with them, together with a few desquamated cylindrical cells.

In another block the lung tissue has broken down forming a small abscess.

Section through another nodule presents a different appearance. Here the process answers to the description of disseminated tuberculosis of the lung. There are discrete and confluent miliary nodules, surrounded by consolidation beyond which is more or less normal lung tissue.

In the center of a miliary nodule is a nearly concentric whorl of coarse, red, coagulated fibrillar material. Surrounding this center is a zone of more loosely lamellated fibrinous material, in the meshes of which are a moderate number of epithelioid and small, round cells. There is

no sharp demarcation between this zone and the necrotic center, and no clear zone of nuclear disintegration except in an early stage, and even then the nuclear fragments are diffused through the whole nodule and there is no karyolysis. Dividing connective tissue nuclei are found in the outer part of this zone, together with numbers of large cells with a single eccentric vesicular nucleus, and fairly abundant protoplasm which takes a bright eosin stain. At the outer margin of the central core, giant cells are occasionally found, with a dozen or more vesicular nuclei placed murally or at the poles of the cell, the protoplasm being abundant, irregular in outline and of a bright red color.

New capillaries and connective tissue cells are abundant between the nodules, the new vessels often being engorged. The nodules contain but few polymorphonuclears. Apparently the nodules are grouped in the neighborhood of a dilated bronchiole.

There is very little pigment deposited along the lymphatics, but disintegrated red corpuscles and blood pigment are found near the foci of coagulation necrosis.

In a section of this block stained with carbol-fuchsin and methylene blue a small number of slender, acid-fast bacilli are found, often beaded, and occasionally slightly branched.

Liver.—Sections of liver stain well; there is considerable irregular contraction and shrinking of the parenchyma cells, especially around the hepatic veins. The parenchyma cells show no pigment, they are coarsely granular and stain deeply in eosin, and are very irregular in size. There is no evidence of cellular infiltration, and no new connective tissue, even where the shrinkage of parenchyma cells is most marked.

Spleen.—The section stains well; capillaries are moderately dilated; the contents in many cases have fallen out; the trabeculæ are somewhat loose and spongy, especially at their margins; the Malpighian bodies are inconspicuous, reduced in size and possibly in number. The sponginess of their reticulum is one factor reducing the prominence of the Malpighian bodies. The bodies contain normal appearing lymphocytes; there is no proliferation. Occasionally, in the center of the Malpighian body, there are found several smaller or larger blocks of bright, red, structureless hyaline material, irregular in size and shape, and apparently free in the tissue. In the neighborhood of such material it is common to find a few of the mononuclears with an increased amount of protoplasm which also has a bright, hyaline-red appearance and which crowds the nucleus to the side.

A focus is found in the pulp resembling an encapsulated solitary tubercle, 2.5 millimeters in diameter. The center is composed of a mass of reddish detritus, mostly granular, with a few fragmenting nuclei. At the periphery is a narrow zone of young connective tissue, advancing toward the necrotic center, apparently devoid of vessels. Surrounding this is a narrow zone of concentric lamellæ, resembling connective tissue,

in the loose meshes of which are rows of small, round cells, usually having irregular nuclei and a few adult connective tissue cells. This zone merges at once into the pulp.

The endothelium of the small arteries is often thickened and irregular, and takes a bright-red hyaline color; the thickening is often uneven, and confined to one-half or less of the circumference of the vessel. This hyaline material appears to be amyloid in the hæmatoxylin and eosin stain, but it does not respond with iodine, iodine and sulphuric acid, nor with methyl violet stains. There is no increase in small, round, cells, nor in polymorphonuclear leucocytes.

Kidney.—The capsule is not thickened; the capillaries and veins are filled with red blood corpuscles; the glomeruli are well preserved, moderately congested, the cells not increased, the capsules of Bowman delicate and normal. The convoluted tubules contain a small amount of granular débris and a fine meshwork of coagulated matter; the lining cells are large, granular, bright red and frequently send protoplasmic fringes into the lumen; the nuclei are near the basement membrane and apparently normal. The loops of Henle and the collecting tubules appear normal. The interstitial tissue is not increased. There are no infiltrating cells.

Pancreas.—The parenchyma cells have retracted from the stroma producing distortions. The cells are small, and rather deeply stained. The islands of Langerhans are normal.

An area is found, miliary in size, having the characteristics of an early tubercle. The nuclei in this area are small, black, fragmenting and irregular; the protoplasm bright-red and hyaline. The area is not sharply marked off from normal pancreas. No karyolysis, no cellular infiltration.

Cervical lymph gland.—In one section the blood vessels are moderately engorged; the lymph channels are widely distended but nearly empty; the stroma is loose and the strands widely separated; the cell nests are not seen, and the cell columns are less dense than normally.

Two areas of necrosis over 1 millimeter in diameter are found. In each case the nodule consists of a large, central mass of bright-red detritus, granular and lumpy, with a few fragmenting nuclei, surrounded by a narrow and imperfect zone of large epithelioid cells with considerable dark-red protoplasm, irregular in shape, and much red-staining interstitial tissue. This zone is free from capillaries and passes over suddenly into lymph gland tissue.

In the peripheral sinus only a few cells are present; several of these are small, with deeply staining nucleus and a narrow band of red protoplasm, taking much the same shade as the erythrocytes. The cells in the internal sinuses are (1) small round cells and (2) large cells with vesicular nucleus and abundant, bright-red protoplasm, apparently desquamated endothelial cells. Many of these are cloudy and have only faint traces of the nucleus remaining. In some cases no nucleus is seen.

In another section the structure of lymph gland is better preserved. The cell nests and cell strands are clearly marked, in contrast to the dilated sinuses which contain many large, pale cells like those described above. There is no endothelioid cell proliferation at the center of the cell nests.

In a section stained with Ehrlich's triacid stain and examined with the oil immersion, the large cells in the sinuses take a diffuse, reddish-purple tint, and show no granulation.

Tissue taken from various parts of the ulcerating area in the nares and prepared by the silver impregnation method of Levaditi do not show spirochætæ, nor other characteristic organisms.

Histological diagnosis.—Necrosis of the nasal passages and adjacent parts; tuberculous nodules in lymph gland, lung, spleen and pancreas, hyaline and amyloid (?) degeneration of spleen; acute bronchopneumonia.

REMARKS.

The only other histological study of this disease which has come to our notice is that of Fordyce. He removed bits of tissue from the edge and center of the ulcer of his case, and made careful studies of specimens stained with various dyes. Although his case resembles ours in many respects, there are several points of difference. In both cases there was an ulcer bordered by tissue showing an infiltration chiefly with small round cells, but also showing numerous plasma cells. In his case there were but few polymorphonuclear cells; in ours such cells were difficult to find. Giant cells, which were fairly numerous in his sections, were absent from ours, although in one section there were proliferating capillaries, which sometimes took the form of a long, vacuolated cell with two or three nuclei. There were no true giant cells in our other sections from the ulcer. In neither case was there caseous degeneration, but in ours, even below where the cellular infiltration was marked, there was diffuse, advancing degenerative change in fibrous, glandular and muscular tissue, which was not present in Fordyce's case. In each, there was hæmorrage into the tissue, which was quite a striking feature of our case, while new forming capillaries, abundant in his case, were noticeably absent from our sections, except under the ulcer at the junction with the skin of the face. Parakeratosis and acanthosis were noted by Fordyce. The epithelial changes in our case, and described above, were similar, but there was not an increase in the horny layer, which was in fact diminished. The epithelial downgrowth in Fordyce's case gave a picture resembling epithelioma (Plate I), a condition which we could definitely exclude.

Summary.—The main differences between these two cases are that in ours there was less reaction, no giant cells, more hæmorrhage, much less granulation tissue formation, and an extension of the necrotising process beyond the line of infiltration into the structures beyond. In

the study of our sections no mast cells were encountered, although plasma cells were abundant. Such differences may readily be due to the variations in the reactive power of different individuals, and to secondary infection and it seems quite probable that the two cases represent the same condition.

III. RÉSUMÉ OF LITERATURE.

There is at the present day some confusion in the differential diagnosis of the various forms of tropical ulceration, and there can be little doubt but that the disease which we treat of in this article has been described at different times under various names. The most complete article dealing with the subject of gangosa which we have found is the recent one by Mink and McLean, and the following summary is taken from this and from the papers of Leys, and of Fordyce and Arnold.

Gangosa was described in 1828 by the Spanish Commission which visited the Ladrone Islands. Similar cases have been reported from the Caroline Islands, Fiji, British Guiana, Italy, Dominica, Nevis and Panama. It probably exists in Ceylon under a different name.[3]

"Gangosa" is a Spanish word and means a "nasal voice." The disease is characterized by a slowly progressing ulceration, starting in the throat, or soft palate, advancing upwards and forwards through the nasal passages, destroying in its progress the septum, hard palate and turbinates, and causing the falling in of the nose. In rather less than 10 per cent of cases the ulceration eventually attacks the anterior nares and leads to more or less complete destruction of the nose, so that it is possible to look through the nose into the mouth and throat. In the later stages the upper lip may be attacked and the process may extend through the lachrymal ducts or across the face to the eyes, leading to secondary inflammations and blindness, the orbit filling up with granulation tissue. Out of eighty-one cases tabulated by Mink and McLean there were only two in whom hearing was affected, while the larynx was involved thirty-three times. In our case there was double *otitis media*. Phonation is always interfered with and the senses of smell and taste are usually lost. It is characteristic that the tongue and muscles of deglutition escape. The ulcers are nearly or quite painless.

In a case reported by Dr. Rat, the ulceration started from a tubercle on the soft palate. Three of Mink and McLean's cases started with mild sore throat or coryza. At first the ulcer is superficial, moveable and covered with a dirty, brownish-gray pelicle. It spreads rapidly, later it becomes chronic and granulation tissue is formed around the base. The ulceration may advance steadily for many years or may become arrested at any time, leaving a chronic ulcer. In most of the cases of Mink and

[3] On a recent visit to the Batanes Mr. Fergusson, of this Bureau, found several colonies of apparently gangotic sufferers living in quarters more or less isolated from the main villages. These people are regarded as lepers.

McLean the ulceration became quiescent after from one to seven years, the average time being two years, while in seven cases the advance was continuous for from ten to thirty-five years. Periods of advance and quiescence may alternate. During quiescence there is an abundant, very offensive discharge. It is remarkable that the general health is hardly affected, even with extensive and long continued ulceration. An exception to this rule is to be noted in the case of children under 5 years, in gangotic families, who may die within forty-eight hours from a fulminating type of the disease, almost like diphtheria. The ulceration in gangosa is limited to the throat and adjacent parts. No similar ulcers are found in other parts of the body.

We had no opportunity to determine the etiological factors in our case. Mink and McLean analyzed 125 cases at Guam and estimate that about two per thousand of the native population are affected, whereas Arnold gives a higher estimate. No cases have been seen in white people or in those of mixed blood. The majority of all cases develop during the second and third decades, and more during the second than at any other equal interval; but the disease may appear at any age from three to sixty or eighty. Women are attacked more frequently than men. Gangosa is not hereditary, but is probably infectious. The natives think that it comes from eating fish. The degree of infectiousness must be low.

Gangosa must be differentiated from other forms of chronic ulceration. Leprosy can be excluded by the absence of nodules, infiltrations and anæsthesia, the fact that the characteristic bacilli can not be found in the ulcer, by the sudden onset of gangosa, and by the general good condition of the patient. From the other granulomata, the differential diagnosis should not be difficult. Epithelioma may be excluded by the wide prevalence of gangosa in a small community, by the early age of onset, the protracted course, the absence of metastases, the softer base of the ulcer and the histological features.

In certain respects the disease resembles an unchecked Vincent's angina or noma. The protracted course and the absence of general symptoms exclude noma. In our case, tissues stained by Levaditi's silver method, by Gram-Weigert and by the carbol-fuchsin methylene blue method for tubercle bacilli failed to show the spirochæta of Plaut and Vincent.

The differential diagnosis from syphilis and yaws is difficult. We do not wish to enter into the syphilis-yaws controversy at this time, and we will merely state that we have never seen any lesions of yaws which presented the faintest resemblance to gangosa, although the typical frambœsial skin lesions are not uncommon in this region. However, it is obvious that gangosa bears a strikingly similar appearance to the ulcera-

tion occurring in syphilis, and Hutchinson [4] has presented a strong case for those who maintain that syphilis and yaws are modified forms of the same disease. Neither Mink and McLean, nor Leys, found any syphilis whatever among the natives of Guam where gangosa prevails so widely and they satisfied themselves that there is no casual connection between syphilis and gangosa. Mink and McLean also convinced themselves that the disease is independent of yaws. Fordyce and Arnold excluded syphilis from the diagnosis of their case, because of the long duration of the ulcer in a limited area, the failure of antisyphilitic remedies to relieve the condition, and because they considered it unusual to have the lachrymal duct involved by direct extension of intranasal syphilitic ulceration. In our case, the patient failed to respond to vigorous antisyphilitic treatment. There were no other signs suggestive of syphilis either clinically or at autopsy, the histological features of the ulcer were not suggestive of syphilis and no spirochætæ could be found in the tissues after impregnation with silver according to the method of Levaditi.

Considering both the literature and our case, we think that the weight of evidence is in favor of the view that gangosa is a disease independent of syphilis, but we do not regard this as a definitely established fact.

Tuberculosis must also be differentiated. In our case the patient had unquestionably a chronic pulmonary tuberculosis with a few small tubercles in various organs, but no tuberculous lesion existed along the advancing edge of the ulcer, and no tubercle bacilli could be found in it. In Fordyce's case the inoculation of guinea pigs and the test with tuberculin proved to be negative for tuberculosis, and, as in our case, the general histological appearances were unlike that disease. At the same time, there were giant cells in Fordyce's sections and in both his and ours there were extravasated red blood corpuscles. According to Stelwagon,[5] lupus not infrequently attacks the mucous membranes, and may affect the soft palate, hard palate, or velum, the mucous membrane involvement taking place in 45 or even 70 or 80 per cent of the cases. Against tuberculosis are (1) the painlessness of the lesion, (2) the long duration, (3) the continued good health of the patient and (4) the absence of symptoms of tuberculosis elsewhere.

The considerations enumerated above dispose us to take the view that this patient suffered primarily from gangosa, apparently a separate disease, that the tuberculous process was secondary and that he died of a terminal acute broncho-pneumonia.

[4] Framboesial Syphilis (Yaws and Parangi); Atlas of Clinical Medicine, Surgery and Pathology of the New Sydenham Society. Part I, Fasciculus XIV (1902).

It will require careful obervations on several cases under prolonged treatment to justify a positive expression of opinion as to the part played by syphilis or yaws in the gangotic process.[6]

REFERENCES.

(1) Fordyce and Arnold: *J. of Cutaneous Diseases* (1906), XXIV, 1.
(2) Leys: *J. Trop. Med.* (1906), IX, 47.
(3) Mink and McLean: *J. Am. Med. Ass.* (1906), XLVII, 1166.

[5] Diseases of the skin: W. B. Saunders, 4th Ed. (1905), 687.

[6] While this article was in press *Stitt* (U. S. Naval Med. Bull. (1907), I, 96) reported a case of gangosa, the first in a white man. The patient, a sailor, had recently come from Guam, where he had exposed himself to gangosa, but he also had a history of syphilis five years before. Antisyphilitic treatment did not check the disease.

ILLUSTRATION.

PLATE I. A photograph showing the deformity of the nose and lip produced by gangosa.

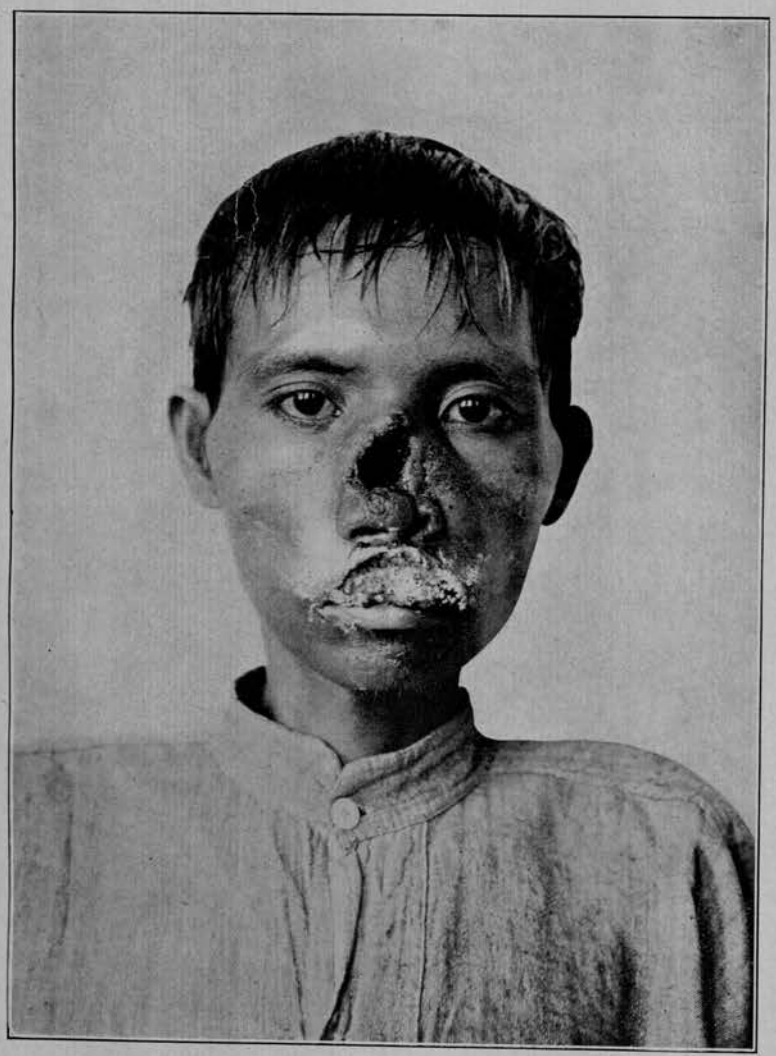


PLATE I.